The New England
Journal of Medicine

Copyright, 1951, by the Massachusetts Medical Society

Volume 244 JUNE 28, 1951 Number 26

RADIATION DAMAGE TO NORMAL TISSUES IN THE DIAGNOSIS AND TREATMENT OF NONMALIGNANT CONDITIONS AND ITS SURGICAL REPAIR*

ERNEST M. DALAND, M.D.†

BOSTON

IRRADIATION in the form of either radium, x-ray or isotopes, is a valuable procedure in the treatment of disease. It is not, however, without its dangers and should always be administered by an expert. In its early days the dangers to the operator and to the patient were not recognized. Today the expert does recognize them, and the men receiving training under him are warned of them. In a search to discover all the possible benefits of irradiation countless conditions were subjected to treatment, and in many it was found of no value. The present generation should have learned of these failures and not be tempted to repeat the experiments.

There is a great difference between using irradiation in treating cancer and in using it to treat benign conditions. In cancer, one is justified in taking great risk of damage to normal tissues, as the one consideration is to destroy the cancer. The trained radiologist has learned to treat many cancers successfully with a minimum damage to normal structures. In benign conditions, one must be sure that the resulting cure is not worse than the disease. There is no justification for causing permanent damage to other tissues when treating benign conditions. Irradiation in malignant conditions is effective because those cells that are immature and more rapidly growing are more sensitive to radiation. The greater the number of undifferentiated cells, the more radiation-sensitive is a tissue.

This paper deals with the unexpected and unwanted effects of irradiation in the treatment of benign conditions. It is a well known fact that the unwise or inaccurate use of irradiation will cause cancer. Here, then, is a weapon used for treating cancer that if used unwisely in benign conditions will produce more cancer. These changes may not occur for a decade or two, but in one case mentioned below the cancer appeared in two and a half years.

Low-voltage x-ray or unscreened radium has been the offender in the greatest number of cases of irradiation damage to the skin. High-voltage x-ray may produce untold damage to normal structures, but there is usually a total destruction, and the same problem of cancer causation is probably not involved. We have rarely observed the occurrence of cancer in areas treated by high-voltage x-ray, and we are led to believe that if proper filters are used cancer will not occur.

Wolbach,[1] as long ago as 1909, described the pathologic characteristics of chronic radiodermatitis in a series of patients operated on by C. A. Porter.[2] In 1924, in another study,[3] he summarized the changes in the skin: complete loss of the appendages of the epidermis, replacement of the normal collagen by a peculiar dense hyaline collagen, obliterative processes in blood vessels of the corium and subcutaneous tissues, necrosis of varying size in the corium, at first in the region of thrombosed telangiectases and reparative proliferation of the epidermis. He further outlined the gradual evolution of a carcinoma in such an area. He also pointed out that changes by irradiation are progressive and irreversible.

I should like to emphasize another area of disease beneath the skin: the subcutaneous fat. In an area of radiation damage there is usually definite loss of fat; this is greatest in the center of the radiated area. When ulceration occurs little, if any, underlying fat remains in that portion of the damaged area. If there is deeper destruction it extends to the fascia, which has a poor blood supply and is easily destroyed.

In the surgical treatment of damaged tissues from irradiation certain facts should be borne in mind:

As much damaged tissue as possible should be removed, down to normal structures.

If no fat remains, thin skin grafts will not be entirely successful and are not as satisfactory as pedicle flaps containing fat. In surgical treatment of fingers thick split grafts are best for good functions, but there is always the likelihood of focal areas of destruction in the grafts.

Wounds from removal of radiated tissue should never be left open to granulate. If such wounds are left open they will soon be covered over by a "scum" of avascular pseudohyalinized tissue. I have seen this happen, whether the irradiation was given a year before or twenty years before. All such wounds should be covered at once.

*Presented at the annual meeting of the New England Surgical Society, Vergennes, Vermont, September 16, 1950.

†Instructor in surgery, Harvard Medical School; visiting surgeon, Massachusetts General Hospital chief of staff, Pondville Hospital, Walpole, Massachusetts.

If there has been deep destruction down to fascia, periosteum or bone, a healthy base may be unobtainable. If the skin and fat of the periphery are normal it is possible to rotate a pedicle flap to cover such a wound, even though the base is very bad. Nourishment to the flap is furnished from the skin edges. Gradually the flap will adhere to the underlying tissues.

Complications of Irradiation

The following case histories illustrate unwanted and unexpected results from irradiation of benign conditions.

Case Reports

Group 1: Damage to the Physician Using Irradiation

Case 1. A 30-year-old physician was seen in May, 1948. Five years previously he had used the fluoroscope to take a foreign body out of a patient's hand. He received an acute burn that was very slow to heal; it had interfered with his work. Recently it began to ulcerate in several small areas (Fig. 1).

Examination showed a total loss of the nails of the first and second fingers on the left, with atrophy, dryness of the skin, loss of fat and telangiectases down to the first interphalangeal joints. On the right hand there was similar damage, but to a lesser degree, over the fourth and fifth fingers, particularly over the middle phalanges.

Figure 1. *Case 1: Hands Damaged by Improper Use of Fluoroscopy in Reducing a Fracture.*

Removal of all the damaged skin over the left hand was carried out, and the fingers were resurfaced with medium-thickness dermatome grafts. Several islands of skin sloughed, but healing was quite satisfactory in four weeks. At that time he left for his home in Venezuela; he has not been heard from since.

The pathological diagnosis was "radiation dermatitis and hyperkeratosis."

Case 2. A 34-year-old veterinarian was admitted in December, 1948. In 1942 and 1943 he very often used a fluoroscopic machine in locating foreign bodies and in reducing fractures in his veterinary work. He then spent two years in military service, doing no radiographic work. On returning to practice he resumed the fluoroscopic work, always wearing leaded gloves. In 1947 his nails became brittle and cracked. In 1948 he developed painful ulcers on his fingers.

Examination showed moderate skin changes over all the fingers of both hands, with numerous areas of hyperkeratosis. Numerous areas of ulceration were seen, but there was no suggestion of malignancy.

The left hand was operated on and all damaged skin removed. It was necessary to remove one fingernail and the nail bed. All the fingers were resurfaced with thick split grafts. Microscopical examination revealed no malignancy.

Comment. Professional men must use the fluoroscope with great caution and always with the protective safeguards that have been developed.

Group 2: Damage to the Patient from Fluoroscopy

Case 3. A 53-year-old man was admitted on February 17, 1948. He had been injured on August 9, 1946, by being struck by a piece of flying metal in the anterior part of the right arm just above the elbow. He was taken to a hospital and an attempt was made to remove the foreign body under fluoroscopic control. The patient thought that the entire procedure took two hours, but the fluoroscope was not functioning during the entire period. About a week later he noticed an area of irritation on the posterior part of the upper arm; this gradually worsened until he was unable to use his arm. A large ulcer appeared, and the pain interfered with his sleep.

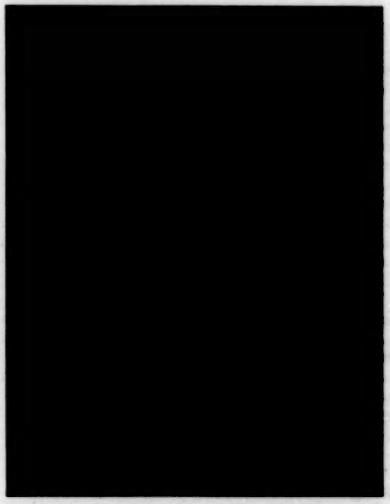

Figure 2. *Case 3: Radiation Damage to Arm from Use of Fluoroscope in Removing a Foreign Body.*

Examination showed an area 6 by 5 cm. over the posterior right arm with redness, numerous telangiectases, leather-like consistency of the skin and a central crusted ulcer 2 cm. in diameter (Fig. 2). All movements of the arm were painful.

A delayed pedicle flap was made on the right side of the abdomen from the front backwards. The ulcer was excised and the flap sutured in place on the arm. There was a good "take" of the flap except for one area from which all necrotic material had apparently not been removed. Three weeks later the flap was divided and the edges sutured to the arm. The other end was resutured on the abdomen. Three other operations were necessary before the small necrotic area had successfully healed.

The pathological report was "Acute and chronic inflammation with ulceration. Hyperkeratosis."

Comment. The fluoroscope is an instrument for the trained radiologist. No others should be allowed to use it. It can be used safely for brief periods only.

CASE 4. A 33-year-old man was admitted on April 17, 1943. This patient attended a meeting during the war at which a physician was giving instruction to a group on first aid. During the meeting the physician mentioned the fluoroscope. After the meeting some of the listeners asked if they could see the fluoroscope. He showed them a portable machine. The patient concerned in this report was used as a demonstrator while about thirty persons watched his heart action through the fluoroscope.

A few days later his back became sore; later an ulceration appeared. The burning and itching interfered with his sleep; he sought surgical relief, as medical remedies had not helped.

Examination showed an area of pigmentation over his back the size of his hand. There were numerous areas of ulceration. Excision and closure was done with a satisfactory result. No disease was found in the tissues removed.

Comment. The fluoroscope is not a toy!

Group 3: Damage to Bone

CASE 5. A 16-year-old girl was admitted on June 29, 1943. At five months of age she had had a large hemangioma at the base of the right thumb. She was treated with radium by a competent dermatologist. He used three 50-mg. tubes of radium, screened with 2-cm. gauze, silver and brass for two hours. The dose was repeated in five months. Telangiectases appeared two years later, but the hemangioma had disappeared. Over a period of years dryness and scaliness of the skin was noted over the treated area, with constant cracking of the skin. The thumb appeared to grow normally until she was ten, after which it seemed not to grow.

Examination showed typical radiation dermatitis over the side of the thumb. This thumb appeared to be about half

FIGURE 3. *Case 5: At Left, Left Thumb with Shortened Phalanges Due to Radium Treatment; at Right, Normal Right Thumb.*

the length of the opposite one. An x-ray film (Fig. 3) showed the terminal phalanx to be half as large as the normal one and the proximal phalanx to be considerably reduced in size. The irradiation had stopped the growth from the epiphyses in these bones.

The involved skin was excised and successfully replaced by a skin graft. No disease was found on microscopical examination.

Comment. Irradiation should never be applied over a growing epiphysis, as further growth will be stopped.

CASE 6. A 19-year-old girl was seen on February 12, 1945, for pain beneath a pigmented mole on her chest wall. Three years previously she had received x-ray treatment for a pigmented nevus (warty, pigmented areas) on the left upper chest. She received a total of 4440 r in four sittings over a period of five months. A 3-cm. cone was used, 200 kv., with a filter of 1 mm. of aluminum, and ½ mm. of copper. One year later, she complained of pain in the region beneath the irradiated mole. X-ray films were read as negative. Nine months later she had a sudden pain beneath the mole and further x-ray films were taken. When the earlier films were reviewed an area of bone destruction in the left second rib was seen, and the films taken nine months later showed a pathologic fracture in the rib beneath the mole. She had discomfort over a period of several weeks, but later x-ray films show that the rib healed completely after the fracture and did not require operation. The pigmented nevus did not disappear. It showed some surrounding radiation reaction. There was localized tenderness beneath the mole and pain on deep inspiration. Eight months later the nevus was excised under general anesthesia. This was reported as a "pigmented nevus." There was no sign of radiation reaction in the nevus itself. This was a benign condition treated with a very large dose of radiation that was sufficient to damage a rib but not to destroy the mole.

Comment. Irradiation is not good treatment for a benign mole. Doses of this size will damage bone and should be used only for malignant conditions.

Group 4: Damage from Treatment of Psoriasis

CASE 7. A 38-year-old man was admitted in November, 1944. From 1921 to 1933 he had been treated for psoriasis of the scalp that later involved the whole body, with little

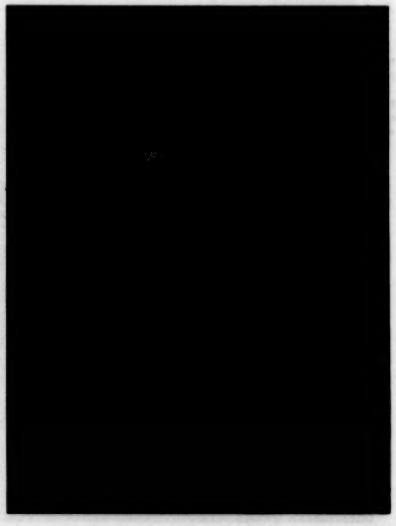

FIGURE 4. *Case 7: Late Radiation Changes in Scalp with Two Areas of Cancer; Late Result of Treatment of Psoriasis.*

improvement. He then went to a skin specialist, who gave him large doses of Fowler's solution and, as results from this treatment were only temporary, decided to use x-ray. The patient received 30 to 40 treatments during the next two years. He then put himself in the care of another physician, who gave him 7 or 8 treatments a year for five years. The patient stated: "While reading a medical periodical I realized the danger of excessive use of the x-ray, and I told Dr.—— to discontinue the use of the x-ray." This was in 1939.

In 1944 an ulcer appeared on the scalp; later a nodule appeared near it. This was burned off and did not reappear, but the ulcer did not heal. Later another nodule appeared farther forward on the scalp.

Examination showed him to be quite bald. The entire exposed dome was covered with atrophic skin, with numerous

FIGURE 5. *Case 10: Result of Depilatory Treatment by X-ray Forty-Three Years Previously. — Carcinoma of Right Eyelid, Eyeball and Preauricular and Submaxillary Nodes and Face.*

telangiectases. The old ulcer due to electrocoagulation was present, and near it was a 2.5-cm. malignant nodule (Fig. 4).

The entire involved scalp was excised down to the periosteum. In two places the periosteum was removed and a shaving of bone was chiseled off. The entire area was covered with a thick split graft taken with a dermatome. The graft was a total loss. Three weeks later a second graft was applied, leaving the bare bone uncovered. This graft was successful.

Microscopically this was revealed as epidermoid carcinoma, Grade III. No lymph nodes were palpable, and no node dissection was done. The patient has been followed for five years; there has been no recurrence.

CASE 8. A 68-year-old woman was first seen in June, 1934. She had been treated for psoriasis for many years. Two and a half years prior to examination she received three x-ray treatments over the knees and two over the elbows at one-week intervals. Five days after the last treatment the knees became black, swollen and painful. She was bedridden for seven months and had excessive pain in the ulcers that appeared. These eventually healed but reopened.

Examination showed extensive changes characteristic of radiation damage over both knees, with large areas of ulceration. On the left knee was noted a nodule that appeared neoplastic.

All damaged tissue over both knees was removed, and the wounds were allowed to granulate for two weeks. Thick split grafts were then applied successfully. On the left there was one area of carcinoma in the center of heavily radiated tissue. She was followed for eight years and had no recurrence of the cancer up to the time of her death. This case has been previously reported.[4]

Comment. X-radiation has been abandoned in the treatment of psoriasis, as the complications were worse than the disease.

Group 5: Damage from Use of Depilatory

CASE 9. A 42-year-old man was first seen in March, 1942. For many years he had had an excessive growth of hair all over his body. That on the dorsum of his hands troubled him particularly. Twelve years before examination he received x-ray treatment (dosage unknown) to the dorsum of each hand. The hair stopped growing. For several years the skin of his hands had been dry and scaly, and an ulcerated area had appeared on the dorsum of the right index finger.

Examination showed a marked radiation dermatitis over the dorsum of each hand, extending well down on the fingers. That portion over the second metacarpal bone and the base of the first phalanx was ulcerated, indurated and obviously malignant.

The patient was on leave from the Army at this time, and it seemed desirable to carry out a minimum operation. The malignant area was excised and a thick split graft sutured in place. Epidermoid carcinoma, Grade I, was the report of the pathologist. Four years later he returned for excision of the damaged tissue over the remainder of the hand. Microscopically no disease was seen. The cancer had not recurred.

Two years later the damaged area on the other hand was excised and the hand resurfaced by another surgeon. Cancer was found in the tissue removed.

FIGURE 6A. *Case 11: Late Changes Following X-ray Treatment for Fungus Infection of Foot.*

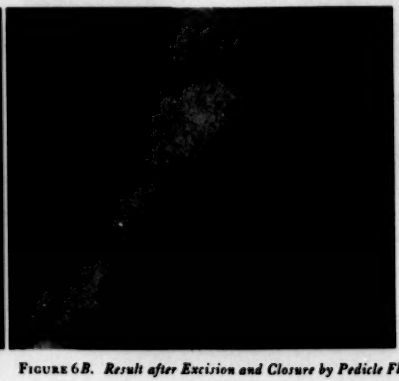

FIGURE 6B. *Result after Excision and Closure by Pedicle Flap.*

CASE 10. A 61-year-old woman was admitted on January 10, 1947. This patient had had x-ray treatment for hair on her face when she was eighteen, — forty-three years before

admission. Her treatment was given by one of the earliest x-ray therapists. She had no trouble for twenty years; she then began to develop telangiectases and dryness of the skin, which began to break down. She received radium treatments from a dermatologist for several years. Later a carcinoma of the right eyelid and conjunctiva developed, for which she was treated unsuccessfully.

When first examined the patient had a cataract of the right eye, persistent cancer involving the eyeball and hard preauricular and submaxillary nodes, in addition to the extensive cancer of the face shown in Figure 5. The cancer was still being treated with radium by a dermatologist, who stated that one small area was suspicious.

Treatment consisted of exenteration of the orbit, removal of positive preauricular nodes, a supraomohyoid dissection of the neck (positive nodes) and removal of the carcinomatous areas of right cheek and chin, with replacement by a tube graft from the chest wall. She has remained free from disease up to September, 1950, but will later need replacement of more skin on the face.

Comment. These are but two of many cases of x-ray carcinoma that we have seen in which superfluous hair has been destroyed by this agent. Suffice it to say that depilatory results cannot be obtained by irradiation without permanent damage to the skin and eventual development of cancer.

Group 6: Damage from Treatment of Fungus Diseases

Case 11. A 21-year-old woman was admitted on June 24, 1944. At the age of nine she had an infection of her fingers, toes and right foot. She was treated with ointments for a time but was given a series of x-ray treatments ten years ago. She had a severe reaction two days after the last treatment. The foot became red and an ulceration appeared. This healed at times, but the patient had constant trouble with the foot. For two years she was unable to walk without crutches, and she had to stop attending school because of pain.

Examination showed an area of radiation dermatitis measuring 8 x 6 cm. in size on the inner aspect of the right foot. Part of the area showed minute ulcers. The foot was contracted and stiff, with all movements limited and painful (Fig. 6*A*).

A pedicle flap was prepared on the left thigh. Two weeks later the damaged area was excised and covered with the thigh flap, with the foot held in position by a plaster spica. The foot was held in this position for nineteen days, after which the flap was divided and sutured in place (Fig 6*B*).

FIGURE 7*A*. *Case 14: Radiation Ulcer of Foot after Excessive X-ray Treatment for a Plantar Wart.*

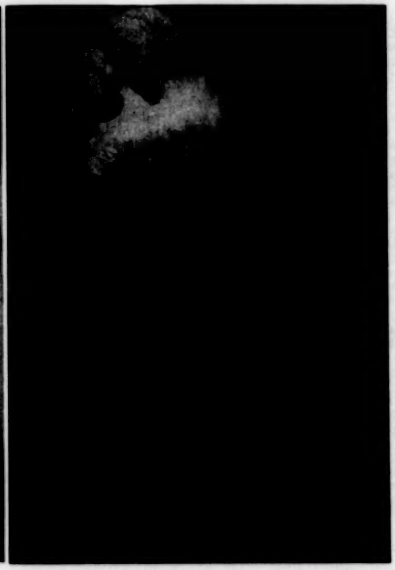

FIGURE 7*B*. *Result after Excision and Closure by Pedicle Graft.*

The relief of pain afforded by the excision outweighed the discomfort of the case during this period. Healing was satisfactory and the foot soon became freely movable. The patient returned to college and was able to play basketball.

Microscopical examination of the excised tissue showed "chronic inflammation and fibrosis."

Comment. The amount of x-ray given this girl is not known. X-ray is a powerful agent for treatment of skin infection; in this case more damage was done than was expected.

Group 7: Damage from Treatment of Plantar Warts

Case 12. A 32-year-old man was admitted on October 6, 1941. He had received x-ray treatment on numerous occasions for two plantar warts on the left foot. In 1935 he had three treatments at one-week intervals. In 1936 he received three more treatments, as one wart had recurred. The wart disappeared but recurred in January, 1941; two more treat-

ments were given. In July, 1941, he had more treatments, which were followed by the development of an acute erythema and an area of painful ulceration. The patient received no relief from ointments.

Examination showed an ulcer 1.2 x 1.4 cm., with a depth of 0.5 cm., on the sole of the left foot. The base was necrotic and painful. The patient walked only with the aid of crutches.

A three-stage excision and closure with a pedicle graft from the right thigh was done. Complete relief was obtained as soon as the flap was applied. There was no question of malignancy in this case.

He served as a naval officer in the Navy for two years, during which period the graft was entirely satisfactory. He developed a similar ulcer on the other foot, which required operation.

Comment. X-ray treatment is proper treatment for plantar warts if given carefully. This case and many others have taught us that repeat treatments are unsafe and lead to serious complications.

CASE 13. A 32-year-old man was admitted on May 11, 1942. This patient had been troubled with a plantar wart for six years. He applied to a hospital for x-ray treatment, where the x-ray technician is said to have treated him without the advice or supervision of the radiologist, who was absent. The patient developed acute redness over the treated area, which was sore for two weeks. For the following two weeks he was quite comfortable, but subsequently the entire treated area became ulcerated. He had been crippled for nine months when admitted, unable to walk or carry on his work.

Examination showed a 4-cm. ulcer with an extreme degree of secondary infection around it. This had the appearance of radiated tissue that had been broken down by infection.

A three-stage pedicle-flap operation was performed and most of the wound successfully covered. A secondary procedure was later carried out for closure of a persistent ulcer on the great toe. Microscopical examination of the excised tissue showed "necrosis, acute inflammation."

He made an excellent recovery, subsequently serving for two years as a naval officer.

CASE 14. A 23-year-old woman was first seen on December 13, 1944. Three plantar warts had been treated by x-ray in a physician's office in August, 1944. A second treatment was given a week later. She was married on the following day. One week after the last treatment her foot became sore; she returned from her honeymoon on crutches. She was treated with sulfa drugs and ointments, without relief. The entire radiated area ulcerated and a deep slough developed. The pain was severe.

Examination showed a deep radiation ulcer 5 x 5 cm. in size over the ball of the right foot. Sloughing was present down to the deep structures (Fig. 7*A*). There was marked rigidity of the toes and much secondary infection.

A pedicle flap was constructed on the opposite thigh. The ulcer was later excised and the defect closed. Healing was complete in ten weeks (Fig. 7*B*). The graft has been satisfactory and the toes have lost their rigidity, although they do not have normal function. The patient has developed troublesome calluses proximal and distal to the flap.

Comment. It seems probable that a larger dose than the one planned was given to this patient. The case illustrates the power of an x-ray machine and the desirability of its being used by an expert.

CONCLUSIONS

X-radiation should be used only by, or under the supervision of, a well trained physician. Repeated doses of low-voltage therapy with improper screening cause permanent damage to tissues. This damage may lead to the development of cancer in the treated area.

Irradiation should not be used when surgery will accomplish as good a result.

It should be avoided in all benign conditions except plantar warts, particularly in the young.

It should not be used in benign conditions over the epiphyses of growing bones.

It should never be used in the treatment of benign moles.

In the treatment of infections or skin diseases, it should be used only by an expert.

It is probably a safe method of treatment for plantar warts, if used wisely. It is never safe to use it a second time. Patients should be told this, so that they will not apply to various physicians for further treatment. Care should be taken that the treated area does not become traumatized or infected.

483 Beacon Street

REFERENCES

1. Wolbach, S. B. Pathological histology of chronic x-ray dermatitis and early x-ray carcinoma. *J. Med. Research* **16**:415-449, 1909.
2. Porter, C. A. Surgical treatment of x-ray carcinoma and other severe x-ray lesions, based upon analysis of forty-seven cases. *J. Med. Research* **16**: 357-413, 1909.
3. Wolbach, S. B. Summary of effects of repeated roentgen-ray exposures upon human skin, antecedent to formation of carcinoma. *Am. J. Roentgenol.* **13**:139-143, 1925.
4. Daland, E. M. Radiation damage to tissue and its repair. *Surg. Gynec. & Obst.* **72**:372-383, 1941.

DIAGNOSTIC IMPLICATIONS OF PERICARDIAL, PLEURAL AND PULMONARY INVOLVEMENT IN CARDIOVASCULAR DISEASE*

LOUIS WOLFF, M.D.†

BOSTON

THE conditions that must be considered in differential diagnosis in patients with a history of chest pain are many. They comprise diseases of the gastrointestinal tract, spinal column, lungs and mediastinum, infections of various sorts, myocarditis, acute myocardial infarction, acute pericarditis, pulmonary embolism and dissecting aneurysm. The greatest difficulty is encountered in differentiating acute myocardial infarction, acute idiopathic pericarditis, pulmonary embolism and dissecting aneurysm. All these conditions are characterized by chest pain, fever, leukocytosis, increased sedimentation rate and an abnormal electrocardiogram. There may be remarkable similarities in these manifestations of the four diseases, but close scrutiny of the history, laboratory data and clinical course furnishes evidence that helps to differentiate them. Nevertheless, differential diagnosis may be impossible. Clinicians are generally familiar with the criteria ordinarily employed in solving the problem, and no attempt will be made here to discuss these well known and proved methods of differential diagnosis. It is my intention, rather, to emphasize how the proper evaluation of evidence of pericardial, pleural and pulmonary involvement may be utilized to make a diagnosis.

PERICARDIAL INVOLVEMENT

The pericardium is or may be the seat of an active inflammatory process in acute idiopathic pericarditis, acute myocardial infarction and dissecting aneurysm but not in pulmonary embolism. Nevertheless, a sound resembling a rub is occasionally heard in cases of pulmonary embolism and is localized to the area of the pulmonic valve. Pericarditis is noted in many other conditions, but these need not concern us here, since it is usually possible to exclude rheumatic fever, tuberculosis, sepsis, lupus erythematosus, uremia and so forth.

Acute idiopathic pericarditis is a benign affection of the pericardium, infectious in nature, and probably of viral origin.[1-4] It is frequently characterized by chest pain that may be similar to that occurring in acute myocardial infarction and dissecting aneurysm. With the onset of pain a pericardial friction rub is audible, or the electrocardiogram displays the characteristic pattern of acute pericarditis. The rub is easily heard and may persist for days or weeks. A characteristic feature of the pain is its aggravation at the very outset by inspiration, cough, bodily motion, swallowing and the recumbent position.

In spite of the active pericardial process, effusion into the pericardial sac does not always occur or is small in amount, although large effusions are occasionally seen. Nevertheless, a conspicuous enlargement of the cardiac silhouette is frequently noted and at times reaches striking proportions. The discrepancy between the enlarged heart shadow, suggestive of a large effusion, and the persistence of cardiac pulsations, though feeble, is noteworthy. If a pericardial paracentesis is done fluid is not obtained, or its amount may be incommensurate with the great increase in heart size. It seems reasonable to conclude that acute cardiac dilatation occurs in some cases of acute idiopathic pericarditis.[1, 5]

Pericardial involvement in acute myocardial infarction is noted in about one fifth of the cases; it occurs when muscle necrosis extends to involve the subepicardial muscle layer and epicardial surface. This rarely occurs at the onset of the attack and usually requires at least twenty-four hours — rarely longer than several days. Evidence of pericardial involvement, therefore, first appears one or several days after the onset of the attack and almost never after the first week. The pericardial friction rub is ephemeral, lasting but a few hours or one or two days at the most. Pericardial effusion usually does not occur in acute myocardial infarction or is insufficient in amount to be recognized clinically. Instances of massive effusion are, indeed, very rare.[6, 7] A persistent rub, or its initial appearance or recurrence after the first week, or the demonstration of pericardial effusion suggests that the diagnosis of acute myocardial infarction is wrong or that if it is correct the lesion is complicated by some other condition. In patients treated with dicumarol the most serious consideration must be given to the possibility of pericardial hemorrhage consequent to hypoprothrombinemia. When this complication occurs oozing of blood may continue for days, resulting in a persistent rub and a large pericardial effusion.[8]

Pericarditis occurs in dissecting aneurysm as a complication of coexisting myocardial infarction or uremia or consequent to hemorrhage into the pericardial sac. The latter, when not immediately fatal, gives rise to the signs of acute pericarditis either at the very onset of dissection or days or weeks later, depending on the time of external aortic rupture into the pericardium. These signs

*From the Department of Medicine, Harvard Medical School, and the Medical Service, Beth Israel Hospital.

†Associate in medicine, Harvard Medical School; visiting physician and consultant in cardiology, Beth Israel Hospital.

are usually persistent or recurrent over a period of days or weeks and are always accompanied by fever and leukocytosis. A slow oozing of blood may be observed for days or weeks; thus, unlike hemorrhage secondary to rupture in acute myocardial infarction, cardiac tamponade and sudden death are not necessarily immediate consequences. Pericardial hemorrhage in dissecting aneurysm is therefore consistent with survival, — at least temporarily, — and the signs of pericarditis may persist for a surprisingly long period. Furthermore, when oozing continues enough blood may accumulate in the pericardial sac to give unmistakable signs of a large pericardial effusion. Fluoroscopy may disclose absence of the cardiac pulsations. Concomitant hemorrhage into the pleura may occur (see below).

Pleural Involvement

The pleura may be actively involved in pulmonary embolism, acute idiopathic pericarditis and dissecting aneurysm but not in uncomplicated myocardial infarction. When the latter is complicated by congestive failure a right-sided or bilateral effusion may occur; this fluid is a transudate and is variable in amount. The pleura is invariably involved in acute idiopathic pericarditis, and is evidenced by a pleural friction rub, progressive thickening of the pleura or pleural effusion.[2] These signs are often bilateral. The fluid is exudative, nonsanguineous and usually but not invariably small in amount. Both pleural and pericardial involvement are noted at the onset or the pericardial precedes the pleural involvement.

Pleural involvement in pulmonary embolism is manifested by pleuritic pain, a pleural friction rub and pleural effusion. Pleural pain occurs in about half of the cases and a pleural friction rub in about one tenth of the cases, but effusion large enough in amount to be readily recognized is uncommon.[9] The effusion, when present, is usually small in amount and may be sanguineous. However, there are rare cases in which recurrent pleural effusions of large amount dominate the clinical picture.

Involvement of the pleura in dissecting aneurysm may occur simultaneously with pericardial involvement, or either one may occur first or one may occur without the other. A characteristic finding is a large left hemothorax, — less commonly a right-sided or bilateral hemorrhagic effusion; when combined with hemopericardium this is strongly suggestive of dissecting aneurysm. A widening of the mediastinal shadow is usually noted when hemothorax is due to aortic rupture, but all other collateral evidence of dissection may be absent. The effusion accumulates more rapidly than, and exceeds in amount, that observed in pulmonary embolism and idiopathic pericarditis. Indeed, the effusion is usually large in amount and recurs rapidly after parencentesis. The first signs of pleural hemorrhage may be dullness and bronchial breathing, without the classical signs of pleural fluid.

Pulmonary Involvement

Pulmonary signs occur in acute myocardial infarction, pulmonary embolism, acute idiopathic pericarditis and dissecting aneurysm. In idiopathic pericarditis signs of pulmonary compression consequent to a pleural or pericardial effusion or signs consequent to pulmonary infection may be observed. Pulmonary edema is rare or nonexistent. In dissecting aneurysm a large pericardial or pleural effusion may give rise to signs of pulmonary compression. Furthermore, since dissecting aneurysm occurs for the most part in subjects with persistent hypertension and hypertensive heart disease, pulmonary congestion may result from congestive heart failure antedating or following dissection, and pulmonary edema not uncommonly occurs after dissection.

Abnormal signs are common at the left lung base in acute myocardial infarction. These consist in a localized patch or patches of crepitant rales, coinciding with plate-like areas observed in x-ray films and interpreted as atelectasis. These signs are so common early in the attack that they may be considered a "normal" finding and not necessarily indicative of such complications as congestive failure and pulmonary infarction or infection. When congestive failure complicates acute myocardial infarction crepitant rales are most commonly found at the right base or are bilateral. Dullness and bronchial breathing may likewise be noted in the presence of atelectasis, but their occurrence requires the consideration of other possibilities, namely, pulmonary consolidation resulting from pneumonia or pulmonary infarction, localized pulmonary edema and a rapidly occurring pleural effusion, consequent to hemorrhage in dissecting aneurysm. Complicating pneumonia is rarely associated with acute myocardial infarction, and pulmonary infarction is unlikely on the first day or two of an illness in previously healthy persons but must be considered after this interval. Localized pulmonary edema, however, is not uncommon in acute myocardial infarction but is usually bilateral and not limited to the left lung base. In addition to dullness or flatness and bronchial breathing, a shower of fine rales during inspiration is often noted; signs of gross congestive failure may or may not be present. The clinical course is usually severe, and frank hemoptysis and marked elevation of temperature and white-cell count may be observed. An erroneous diagnosis of pneumonia or pulmonary infarct is common. The x-ray picture is diagnostic.

The pulmonary signs in pulmonary embolism, unlike the "normal" findings in myocardial infarction, are not common in the left lung base. They are found anywhere, although most commonly

at the right base. They are due to atelectasis or pulmonary infarction; they include localized crepitant rales, dullness and bronchial breathing. Intense dyspnea, in the absence of abnormal pulmonary signs and, indeed, of abnormal cardiac signs, is occasionally observed.

The classical signs of frank pulmonary edema or asthma may occur in acute myocardial infarction, pulmonary embolism and dissecting aneurysm but not in acute idiopathic pericarditis.

Case Reports

Case 1. B. S. (B. I. H. M6344), a 66-year-old man, was admitted on May 30, 1949, after the sudden onset of severe crushing anterior chest pain with radiation to both shoulders and forearms. Similar but fleeting pain, provoked by effort and relieved by rest, had been present during the previous four weeks.

Examination disclosed a critically ill man who was gasping for breath. The skin was cold, moist and ashen gray. The blood pressure was 110/70, having fallen from a level of 168/90 prior to admission. The neck veins were engorged and fine crepitant rales were audible at the right lung base as high as the seventh intercostal space. The liver was enlarged and there was minimal pitting edema of both legs and over the sacrum. The heart sounds were of poor quality. The electrocardiogram showed right-bundle-branch block, and extensive myocardial injury and necrosis in the anterior wall of the left ventricle. A diagnosis of acute myocardial infarction with congestive heart failure was made, and digitalis, mercurial diuretics and dicumarol were administered.

Clinical course. The patient was in a precarious condition for seven days but then improved and made an excellent recovery. On June 1 bronchial breathing was audible at both lung bases, and flatness and absent tactile fremitus were noted at the left base. Paracentesis, however, yielded only 2 or 3 cc. of straw-colored fluid. On the following day respiratory distress was more marked, and there was persistent cough with production of large amounts of brown or pink sputum. A shower of fine inspiratory rales was now audible at both lung bases, more marked on the left. The prothrombin activity on June 3 was 2.0 per cent of normal, hemoptysis and hematuria were noted and a pericardial friction rub appeared and persisted for ten days. Dicumarol was temporarily omitted, and the hypoprothrombinemia was treated with fresh plasma and vitamin K administered intravenously. The bronchial breathing had disappeared on June 6, but crepitant rales were still present at the right lung base and over the entire lower half of the left lung posteriorly. Basal rales and sacral pitting edema were still present on June 20 but from then on gradually disappeared.

Comment. There can be no question concerning the diagnosis of acute myocardial infarction. On admission there were definite signs of congestive failure, and the crepitant rales at the right base were interpreted on this basis. Subsequently the bilateral bronchial breathing, the signs suggestive of fluid at the left base and the persistent pericardial friction rub made it necessary to consider other possibilities: dissecting aneurysm coexisting with myocardial infarction, hemorrhagic pericarditis secondary to dicumarol therapy, pulmonary infarction or infection, and localized pulmonary edema.

Since left hemothorax following chest pain is an important diagnostic sign of dissecting aneurysm, especially in the presence of pericarditis, a pleural paracentesis was carried out. The negative tap and x-ray examination, however, excluded pleural fluid, and the roentgenologist made a diagnosis of localized pulmonary edema. The subsequent evolution of the signs confirmed this interpretation.

A persistent pericardial friction rub is rare in uncomplicated myocardial infarction but is consistent with acute idiopathic pericarditis, dissecting aneurysm and hemorrhagic pericarditis consequent to dicumarol therapy. Idiopathic pericarditis was readily excluded by the characteristic electrocardiographic signs of muscle necrosis, and there was no collateral evidence of dissecting aneurysm. Hemorrhagic pericarditis could not be excluded, and treatment as indicated above was instituted.

Case 2. B. B. (B. I. H. 46949), a 66-year-old woman, was admitted on December 12, 1944, soon after the onset of anterior-chest oppression, weakness, collapse and dyspnea. She had had hypertension for thirty years and angina pectoris for three years. On a previous hospital admission in 1939 it was noted that the blood pressure was 240-170/140-110 and that the heart was enlarged.

Examination on admission disclosed a restless, cyanotic, dyspneic, partly unresponsive woman complaining of pain in the chest and head. The blood pressure was 90/60, the heart was enlarged and a harsh systolic murmur was heard at the apex and the aortic-valve area. A few crepitant rales were audible at both lung bases. The neurologic examination was negative. An electrocardiogram showed paroxysmal auricular tachycardia at a rate of 120 and an independent ventricular rhythm at a rate of 62. The white-cell count was 36,400. A diagnosis of acute myocardial infarction was made, and 500 cc. of plasma was given intravenously.

On the following day dullness, increased tactile fremitus and bronchial breathing were found at the left lung base. A chest film showed a homogeneous ground-glass haziness of the left lung field, a coating arrangement of pleural fluid about the upper half of the lung and a markedly enlarged upper-mediastinal shadow, with displacement of the trachea to the right. Paracentesis of the left chest yielded 400 cc. of grossly bloody fluid, and a diagnosis of rupture of the thoracic aorta with left hemothorax was made. Five hundred cc. of hemorrhagic fluid was removed on the following day. Despite transfusions of whole blood, the patient died on December 15.

Autopsy (A-44-120) disclosed dissecting aneurysm of the ascending thoracic aorta, with rupture into the mediastinum. The entire mediastinum was full of clotted blood, and posteriorly the mediastinum bulged out into both pleural cavities, especially the left. The right and left pleural cavities contained 125 and 375 cc. respectively of dark-red blood. The pericardium was normal, and the heart weighed 408 gm. Fresh thrombi were found in two branches of the left circumflex and in the main stem and a distal branch of the right coronary artery. Histologic sections revealed fresh myocardial infarction.

Comment. The admission diagnosis of acute myocardial infarction was not questioned until the abnormal signs at the left lung base were detected. The signs were characteristic of pulmonary consolidation or of a rapidly accumulating effusion such as occurs when hemorrhage is the cause of the effusion. The latter possibility suggested the diagnosis of dissecting aneurysm and was an indication for pleural paracentesis. There were no other clinical signs of dissecting aneurysm, although subsequent x-ray examination revealed a markedly widened mediastinal shadow.

The multiple acute coronary thromboses and myocardial infarction found at autopsy were, in all probability, secondary to shock consequent to dissecting aneurysm with rupture.[10]

Case 3. S. B. (B. I. H. M5968), a 68-year-old woman, was admitted on May 10, 1949. Diabetes was first noted in 1942, at which time the blood pressure was 220/140. The diabetes was controlled by diet and insulin, and the blood pressure subsequently ranged between 170/110 and 210/130. Cardiac enlargement and a basal systolic murmur were noted several years before the onset of the present illness. A milk leg had been present since childbirth many years previously.

The present illness began on April 14, 1949, with malaise, cough and nausea. Examination disclosed a red throat and a temperature of 101°F.; penicillin was given for three days. On April 18 precordial discomfort appeared for the first time, and the blood pressure dropped to 160/80. An electrocardiogram was normal, but the attending physician made a diagnosis of acute myocardial infarction, and bed rest was continued. Recovery seemed complete at the end of three weeks, and ambulation was started. That night precordial discomfort recurred, and the patient was restless. On the following morning, — May 7, — a spell of weakness occurred, and examination showed pallor, sweating, a blood pressure of 140/90 and transient auricular fibrillation

with a ventricular rate of 120. Bed rest was resumed. Examination on May 8 disclosed a temperature of 99.6°F., pallor, a to-and-fro pericardial friction rub over the lower sternum and dullness and crepitant rales at both lung bases. An electrocardiogram was identical with the previous one.

There was considerable subjective improvement on May 9, although pain under the upper sternum, especially on inspiration, was still present. The patient looked well, the skin was hot and dry, the pulse rate was 110 and regular and the blood pressure was 150/80. Auscultation disclosed a to-and-fro pericardial friction rub along the left sternal border. Dullness, decreased vocal and tactile fremitus, bronchial breathing and egophony were noted at the left base. The right leg was markedly swollen (milk leg), and the left showed slight pitting edema, fullness of the veins and calf tenderness. No Homans sign was observed. All peripheral pulsations were normal.

A diagnosis of hypertensive heart disease, paroxysmal auricular fibrillation, pulmonary embolism and infarction, pericarditis of unknown etiology and deep phlebitis of the left leg was made.

She was admitted to the Beth Israel Hospital on May 10. Fluoroscopy revealed left pleural effusion and a water-bottle configuration of the cardiac silhouette, with absence of pulsations. The white-cell count was 30,200. A diagnosis of dissecting aneurysm with rupture of the aorta into the pericardium and left pleural cavity was made despite the absence of other signs of this condition.

Clinical course. Auricular fibrillation continued with short intervals of regular sinus rhythm and digitalization was carried out. The pericardial friction rub persisted, and the heart sounds grew progressively weaker. Several electrocardiograms were normal except for auricular fibrillation and digitalis T-wave changes. Tachypnea and slight dyspnea developed, and the dyspnea became so severe on May 13 that a left pleural paracentesis was carried out. After the withdrawal of 600 cc. of blood-tinged fluid the procedure was discontinued because of cough. The patient died on May 14.

Autopsy (A-49-45) disclosed a Y-shaped tear in the aorta several cm. above the aortic valve, leading into the pericardial cavity. The pericardium was markedly distended, with firm, adherent, grayish-red blood clots, which were serous in some portions. The right and left pleural cavities contained 150 and 75 cc., respectively, of serosanguineous fluid. The heart was enlarged and showed fibrosis and calcification of the aortic leaflets and of the aortic leaflet of the mitral valve and minimal thickening and fusion of the chordae tendineae of the mitral valve. The coronary arteries were calcified and narrowed, but the myocardium appeared normal.

Comment. This case illustrates well the difficulty of determining the cause of chest pain and the diagnostic implications of pericardial, pleural and pulmonary involvement in cardiovascular disease. The original diagnosis of acute myocardial infarction was apparently made on the basis of prolonged chest pain, fever and drop in blood pressure in an elderly woman with hypertension and diabetes. Symptoms of an upper-respiratory infection may occasionally precede acute myocardial infarction but are much more common in acute idiopathic pericarditis. Diagnosis of the latter, however, cannot be made in the absence of both the pericardial friction rub and the characteristic electrocardiographic pattern of acute pericarditis. On the other hand, the diagnosis of acute myocardial infarction is open to suspicion when the electrocardiogram is normal. No diagnosis could have been made, with the available evidence, during the first phase of this patient's illness.

The correct diagnosis should have been made at the beginning of the second stage of the illness (May 9). Dissecting aneurysm was considered, in fact, because of the pericardial friction rub and signs of left pleural effusion, but the signs of phlebitis were misleading and, in conjunction with the chest signs, led to the incorrect diagnosis of pulmonary embolism. The three-week period of immobilization in a 68-year-old woman with vein disease appeared to favor this diagnosis. That is, the possibility was considered that acute idiopathic pericarditis was the primary disease, complicated by pulmonary embolism consequent to immobilization. The premonitory signs of infection and the benign course of the illness up to this point were characteristic of, and the physical findings were consistent with, acute idiopathic pericarditis.

Only after fluoroscopy was the diagnosis of dissecting aneurysm made with assurance. Absent cardiac pulsations are not often observed in acute idiopathic pericarditis, and more pleural fluid was noted than is commonly found in pericarditis or pulmonary embolism. The subsequent demonstration of left hemothorax strengthened the diagnosis of dissecting aneurysm. In retrospect, evidence of pericardial involvement was first noted three weeks after the onset of pain, a sequence consistent with dissecting aneurysm but unexpected in acute idiopathic pericarditis.

TABLE 1. *Pericardial, Pleural and Pulmonary Involvement in Cardiovascular Disease.*

	Pericardial Involvement	Pleural Involvement	Pulmonary Involvement
Pulmonary embolism	None	Pleuritic pain in 50% of cases Rub in 10% of cases No or little effusion; may be sanguineous	Common
Acute idiopathic pericarditis	At onset, persistent Effusion small when present Cardiac pulsations preserved	In all cases; may be bilateral Effusion, when present, small, non-sanguineous	Rare
Dissecting aneurysm	At onset or later, recurrent or persistent Large hemorrhagic effusion, with absence of pulsations	Left hemothorax at onset or later Large effusion With or without pericardial involvement	Common
Acute myocardial infarction	Early, transient No effusion	None	Common
Hemorrhagic pericarditis secondary to hypoprothrombinemia in acute myocardial infarction	Early or late, transient, recurrent or persistent Large hemorrhagic effusion	None	Common

CASE 4.* A 37-year-old man with a two-year history of episodes of substernal discomfort accompanied by dizziness was admitted to another hospital complaining of substernal pain and pressure radiating to the back of the neck of seven hours' duration. The pain was intensified by inspiration from the outset.

Examination revealed impaired resonance, diminished breath sounds and scattered sibilant rales at the right lung base. The heart was normal on examination, and the blood pressure was 124/84.

Laboratory data. The white-cell count on entry was 15,750; it declined gradually, reaching normal on the sixteenth hospital day. The sedimentation rate was at first markedly elevated and did not attain normal values thereafter. Seven electrocardiograms were obtained, the first one on the second day of illness and the last one four or five days before death. They were all abnormal.

Clinical course. The temperature ranged up to 101°F for the first three or four days and then gradually returned to normal, remaining so except as noted below. Pain was controlled with morphine sulfate, but several minor episodes of substernal pressure associated with dyspnea subsequently

*Data furnished by Dr. M. Brown.

occurred. Severe precordial pain and weakness and a sharp rise in temperature occurred on the twenty-fourth day, after which the heart sounds became distant, and a systolic murmur was heard all over the precordium. A similar attack occurred five days later, after which impaired resonance and breath sounds were noted at the left lung base, but thoracentesis yielded only 40 cc. of turbid yellow fluid. A loud, widespread pericardial friction rub was first heard on the sixth day of the illness; it persisted for four to five days. The patient died suddenly on the thirty-third day of illness.

The essential post-mortem findings were rupture of the aorta into the percardial sac, which was bulging with fresh and old blood, and old and organizing pericarditis. There was no coronary disease, myocardial infarction or muscle necrosis.

Comment. The clinical picture seemed entirely consistent with acute myocardial infarction, which diagnosis was actually made. The abnormal electrocardiograms and pericardial friction rub appeared to confirm this diagnosis. However, it should have been excluded, since pericarditis was evident at the very outset of the attack as evidenced by the symptoms and persisted for at least twelve days, as demonstrated by the electrocardiogram and friction rub. In addition, the electrocardiograms disclosed no evidence of muscle necrosis. The only diagnosis that was warranted by the available evidence was acute pericarditis. Intensification of the pain by inspiration at its very onset, in addition to the characteristic electrocardiographic findings, indicated this diagnosis and no other. The problem was to determine its cause. Rheumatic fever, sepsis, tuberculosis, lupus erythematosus, uremia and so on could be excluded, leaving for consideration acute idiopathic pericarditis and dissecting aneurysm.

The diagnostic field having been restricted to these two conditions, the correct diagnosis might have been made by pursuing three lines of investigation: fluoroscopy, pericardial paracentesis and a careful search for collateral signs of dissection aneurysm. Fluoroscopy would probably have disclosed absent cardiac pulsations, and paracentesis would have yielded grossly bloody fluid, thus favoring the diagnosis of dissecting aneurysm.

Case 5. H. R. (B. I. H. 98859), a 42-year-old man, was admitted with severe substernal pain of one hour's duration. Examination disclosed poor heart sounds, a blood pressure of 95/65 and fine crepitant rales at both lung bases. An electrocardiogram disclosed acute muscle injury in the posterior wall of the left ventricle. A diagnosis of acute posterior myocardial infarction was made, and dicumarol therapy was started.

Clinical course. A pericardial friction rub was noted on the third hospital day and persisted until the twelfth day, after which it was no longer audible. On the fifteenth day anterior chest pain occurred and was followed by a drop in blood pressure, which had risen from the initial level to 90/80. More profound collapse was noted on the following day, and all the superficial veins were distended. The prothrombin time was 67 seconds; 100 mg. of menadione bisulfate and 200 cc. of stored plasma were given intravenously. The patient failed to respond and died on the sixteenth hospital day.

Autopsy showed acute and healing posterior myocardial infarction, hemorrhagic pericarditis and cardiac tamponade. Careful examination failed to reveal myocardial rupture or tear of a blood vessel.

Comment. The persistence of a pericardial friction rub is unusual in myocardial infarction; it suggests the occurrence of some complication, concomitant dissecting aneurysm with rupture into the pericardium, or an error in diagnosis. Experience with this and other cases[8] indicates that patients with acute myocardial infarction who have been treated with dicumarol may develop hemorrhagic pericarditis, especially when the prothrombin activity is unduly depressed; suspicion should be aroused if a pericardial friction rub persists or first appears or returns after the first week of the illness or if pericardial effusion is demonstrated. Pain, drop in blood pressure and high venous pressure may indicate profuse hemorrhage and cardiac tamponade. Prompt treatment may be life-saving.

Case 6. S. B., a 30-year-old man, was awakened by severe anterior constricting chest pain during convalescence from a grippe-like infection. The pain was markedly accentuated by bodily movements and inspiration; hypodermic injection of morphine was necessary for relief. Examination made a few hours after the onset of pain disclosed an oral temperature of 101°F., diminished respiratory excursion of the left lower chest and a loud pericardial friction rub; the blood pressure was 142/76.

Laboratory data. The white-cell count was 14,300 on one occasion but was otherwise normal. Serial electrocardiograms displayed elevated ST segments and inverted T waves and final reversion to normal. X-ray films disclosed considerable enlargement of the cardiac silhouette, with normal ventricular pulsations; the heart shadow gradually became smaller and was almost within normal limits at the end of four weeks. Thickening of the pleura at the right and left lung bases and small bilateral pleural effusions were noted.

Clinical course. The temperature spiked to 104°F. daily for twelve days, subsequently reaching normal levels. The pulse rate averaged 85, and the blood pressure remained essentially unchanged. The pericardial friction rub was audible for fifteen days. Slight dullness and crepitant rales were noted at both lung bases on the fourth day, and a few days later a small area of bronchial breathing at the right base was detected. The pain rapidly subsided, but cough was very troublesome for a number of days. Recovery appeared to be complete at the end of thirty days.

Comment. The location and character of the pain were consistent with acute myocardial infarction, acute idiopathic pericarditis, dissecting aneurysm and pulmonary embolism. The attending physician made a diagnosis of acute myocardial infarction, but the accentuation of pain by bodily movements and inspiration at the onset of the attack, the immediate appearance of a pericardial friction rub, the diminished respiratory excursion of the left lower chest and the bilateral pleural effusion should have suggested other possibilities. The persistence of fever and the pericardial rub, likewise, were not characteristic of acute myocardial infarction.

The simultaneous involvement of the pericardium and pleura at the onset of the attack and the continuing involvement of these structures were consistent with dissecting aneurysm, provided that hemorrhagic effusion into the serous cavities could be demonstrated. Since the heart shadow became progressively smaller while the pericardial friction rub persisted, it was deemed unnecessary to perform a paracentesis. Furthermore, careful search revealed no collateral signs of dissecting aneurysm.

Pulmonary embolism was excluded in the very beginning because of the pericardial involvement but had to be considered later as a possible complication when pulmonary signs and small bilateral pleural effusions were observed. Roentgenologic study disclosed none of the characteristic findings of pulmonary infarction, and electrocardiograms failed to reveal the pattern of acute cor pulmonale.

All the findings were consistent with acute idiopathic pericarditis: the onset of pain after a respiratory infection, the immediate evidence and persistence of pericardial involvement, the simultaneous involvement of the pleura, the small bilateral pleural effusions and the striking increase in the size of the cardiac shadow with preservation of good ventricular pulsations. The pulmonary signs were probably attributable to pulmonary infection, which is occasionally seen in this condition. The electrocardiogram was characteristic of acute pericarditis and displayed none of the signs of myocardial necrosis seen in cases of acute myocardial infarction.

Summary

The diagnostic implications of pericardial, pleural and pulmonary involvement in cardiovascular disease have been discussed; illustrative cases have been presented.

Pericardial involvement in acute myocardial infarction occurs between the second and seventh days. The signs are transitory, and effusion does not occur; active pleural involvement is not noted, but pulmonary signs are common. In cases treated

with dicumarol, persistence of a pericardial friction rub or its initial appearance or recurrence after the first week and evidence of pericardial effusion suggest hemorrhagic pericarditis secondary to hypoprothrombinemia.

Acute idiopathic pericarditis is distinguished by evidence of pericardial involvement at the onset of pain; effusion does not occur or as a rule is small in amount; the signs persist for days or longer and then disappear. Pleural involvement, often bilateral, is noted in all cases and is usually evident from the beginning. Pleural effusion, except in rare instances, is small in amount. Pulmonary signs are uncommon.

A characteristic feature of dissecting aneurysm is the presence of large pericardial and pleural hemorrhagic effusions. Such involvement may occur with the onset of pain or days or weeks later; it may be persistent or recurrent. Pulmonary signs are common.

In pulmonary embolism, pulmonary and pleural signs are common. Pleural effusion is usually small and may or may not be hemorrhagic. Pericardial involvement does not occur.

There are many other signs of proved value; these are of the utmost importance in the differential diagnosis of cardiovascular disease and must not be neglected. Those discussed here have not been adequately emphasized in the past. Their careful consideration greatly enhances the possibility of correct diagnosis. Furthermore, involvement of the structures referred to, if not properly evaluated, may lead to erroneous conclusions.

Cases 2, 3 and 6 were seen through the courtesy of Drs. H. Morrison and H. Molliver.

270 Commonwealth Avenue

References

1. Barnes, A. R., and Burchell, H. B. Acute pericarditis simulating acute coronary occlusion: report of fourteen cases. *Am. Heart J.* **23**:247-268, 1942.
2. Wolff, L. Acute pericarditis simulating myocardial infarction. *New Eng. J. Med.* **230**:422-425, 1944.
3. Burchell, H. B. Acute nonspecific pericarditis. *Mod. Concepts Cardiovasc. Dis.* **16**: March, 1947.
4. Cossio, P., and Berconsky, I. Pericarditis aguda benigna. *Medicina* **7**:1-20, 1947.
5. Wolff, L. Acute pericarditis with special reference to changes in heart size. *New Eng. J. Med.* **229**:423-431, 1943.
6. Schwartz, S. P. Pericardial effusion following acute coronary vessel closure. *Am. Heart J.* **10**:253, 1934.
7. Smith, H. L., and Willius, F. A. Pericarditis. III. Pericarditis with effusion. *Arch. Int. Med.* **50**:192-202, 1932.
8. Goldstein, R., and Wolff, L. Hemorrhagic pericarditis in dicumarol treated cases of acute myocardial infarction. *J. A. M. A.* **146**:616-621, 1951.
9. Sagall, E. L., Bornstein, J., and Wolff, L. Clinical syndrome in patients with pulmonary embolism. *Arch. Int. Med.* **76**:234-238, 1945.
10. Blumgart, H. L., Schlesinger, M. J., and Zoll, P. M. Multiple fresh coronary occlusions in patients with antecedent shock. *Arch. Int. Med.* **68**:181-198, 1941.

SPRAIN-FRACTURES OF THE ANTERIOR LIP OF THE OS CALCIS*

CHARLES H. BRADFORD, M.D.,† AND IVAR LARSEN, M.D.‡

BOSTON

IN 1931 Dachtler[1] presented a study of 26 cases of "fractures of the anterior, superior portion of the os calcis due to indirect violence." This was followed by a report published independently by Christopher[2] in which he suggested that these fractures might be a "common injury which deserves recognition as a definite clinical entity." These fractures have been overlooked in the literature since that time, except for a recent excellent article by Gellman.[3] Nevertheless, the injury is not uncommon. Two years ago this injury was called to our attention; since then we have seen 26 cases in our clinics and have been consulted in 5 others, treated by our associates. The chief message of the present paper is to warn practitioners of the need for recognizing and treating this fracture early in order to avoid prolonged disability.

Clinical Characteristics

The clinical characteristics of these injuries are usually clearly distinguished if observers will take the trouble to look for them. The original accident is generally a fall that may involve either acute dorsiflexion of the foot or acute equinovarus strain. Pain may follow immediately, but often it is not severe enough to be disabling. Examination at the onset or subsequently will reveal one sign that is constant. This is an area of sharply localized and acute tenderness, just below the level of the tip of the lateral malleolus, and approximately two finger-breadths anterior to it; that is, precisely over the junction of the os calcis with the cuboid. This location is not far from that of a "Jones fracture" of the proximal head of the fifth metatarsal but is readily distinguished from the latter injury. A careless examiner will often miss the diagnosis by reporting generalized pain in the midtarsal region of the foot, characteristic of a sprain. Too often, these patients are treated with strapping or with the simple advice to soak the foot in hot water and "go easy." They may continue, with increasing disability, for a week or ten days until exaggerated pain develops, out of all proportion to the trivial onset of the symptoms. The calf muscles may be affected; one patient described her sensations as similar in character and location to the sharp pain she had felt when her

*From the Bone and Joint Service, Boston City Hospital, and Orthopedic Department, Boston University School of Medicine.

†Assistant professor of orthopedics, Boston University School of Medicine; visiting physician, Boston City Hospital.

‡Staff member, The Queen's Hospital and Children's Hospital, Honolulu, T. H.; associate surgeon, Shriners' Hospital, Honolulu; formerly, fellow, Orthopedic Service, Boston City Hospital.

plantaris tendon ruptured several years previously. Even a sympathetic physician, if not already familiar with the condition, is likely to suspect a neurotic background at this stage. However, recurrence of this same acute clinical picture in many of our patients shows that the complaints are genuine. Total disability may persist four, five or six months because of the unreasonable amount of pain from weight-bearing. Although Dachtler believed that eventual recovery was assured within six months, Christopher described persistence of pain in one of his cases for eighteen months.

Roentgenographic Characteristics

Roentgenograms are reported as negative in many cases, despite the presence of the fracture. There are three reasons for this error. The fracture

Figure 1. *Lateral View Showing Fracture of Anterior Lip of Os Calcis.*

itself may be inconspicuous, having little displacement and showing only a linear shadow across the anterior lip of the os calcis. Furthermore, unless the foot is tilted into moderate varus and equinus, the head and neck of the talus will obscure the lateral view by overshadowing the zone of the fracture (Fig. 1). This can be brought into sharp relief against an unshadowed background by fully opening the sinus tarsi with inversion and plantar flexion of the foot. However, the fracture may not show at all in the lateral view, and careful anteroposterior views of the foot, throwing the lateral border of the anterior process of the os calcis into silhouette, will be necessary for complete study (Fig. 2). Another confusing point is the rare possibility of an anomalous bone in this area (calcaneus secundarius), giving an appearance of a fracture. The smooth edges and rounded appearance of the anomaly help to differentiate it, together with the history of trauma and the localization of signs and symptoms.

Mechanism of Injury

It will be recalled that the cubocalcaneal joint lies in a vertical plane with the anterior lip of the os calcis tending to curve above the cuboid. If the patient slips and falls forward, further dorsiflexion

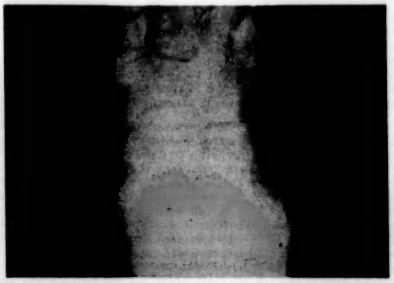

Figure 2. *Anteroposterior View Showing Avulsion Fracture of Anterolateral Border of Os Calcis.*

may impact these two bones so heavily that the lip of the os calcis is broken off. A simple and common illustration of this mechanism is shown in one of our patients, a woman who caught her heel on a low curbing while her body weight pitched forward, thus forcing the front portion of the foot into sharp dorsiflexion. The essential causative principle of this fracture, therefore, seems to be that dorsiflexion of the foot, like pride, goeth before the fall. But this is not true in all cases. The very opposite mechanism, that of forced equinovarus, sometimes causes an avulsion fracture in the same region. If the anterior portion of the foot is plantarflexed and internally rotated, the articular ligaments may carry away a small, discrete portion of the calcaneal lip. An example of this type can be cited from one of our recent cases in which a fireman, sliding down a pole, landed violently on the outer side of his forefoot, which was thus forced into extreme varus and plantar flexion.

The fracture itself probably represents only a small part of the damage associated with this injury, for undoubtedly the sprain that accompanies it contributes largely to the disability. The authors have seen four such sprains without fracture, in which the subsequent clinical course closely paralleled that of the anterior-lip fractures.

Case Reports

Those patients who received adequate treatment at the start recovered relatively fast. In our series, there were 17 such cases; the average length of disability ran about 7.5 weeks. However, if treatment was inadequate or neglected during the pri-

mary stage, the average disability lasted four to six months. There were 9 such cases in our series. The summaries of three of them are illustrative:

Case 1. D. S., a 33-year-old woman, was injured by a fall from steps; the mechanism is not definitely known. Immediate symptoms were mild; she continued work for a week. Pain increased. The industrial physician gave her novocain injections and strapping and encouraged activity. She attempted work, rested five days, attempted work again for two days; she was obliged to stop. X-ray films showed fracture. Complete rest was ordered, with heat and soaking at home, elastic bandage, crutches and no weight-bearing. She was unable to return to work for three months. Her condition was improved, but she was still lame at that time. X-ray films showed fracture healing, and she resumed light work. Recovery was complete after six months.

Case 2. L. C., a 32-year-old woman, fell on stairs, caught her heel and tumbled forward. Pain was mild at first. Aching began on the following evening but she continued housework for two weeks. She felt a "snap" in the foot; thereafter pain rapidly became unbearable. Diagnosis was made of fracture to the anterior lip of the os calcis, but x-ray films at first failed to show fracture. Fresh views revealed it in anteroposterior projection. Treatment was as described in Case 1. There was very little improvement for six weeks. At ten weeks definite gradual improvement was recognized, but she was still unable to tolerate weight-bearing. At the end of fifteen weeks, symptoms had essentially cleared except for weakness and very slight pain. X-ray films made at this time showed healing of the fracture.

The final summary illustrates the one case we have seen of a permanent partial disability.

Case 3. M. McS., a 28-year-old woman, stated that six years previously she had jumped into a snowbank, slipped, and fallen to the ground, but she did not recall the exact manner of her fall. There was immediate pain in the foot. She was treated at a hospital. Extensive sprain was evident clinically, and a small chip fracture was found on x-ray examination. She was given adhesive strapping and crutches; she did not return to the hospital for follow-up study. Pain and swelling gradually subsided, but chronic weakness and some tenderness persisted. At present, x-ray films show nonunion of fracture. Inversion of the foot is painful at the site of fracture, and this area is tender. Pain develops if the patient attempts work involving standing for long hours or much walking, and she has difficulty walking on rough ground. She has been obliged to give up dancing because of pain. She refused operation when it was suggested but said that if the pain became worse she would consent. She will continue under observation another year.

It is of interest that there were twice as many female as male patients. This might be traced to the shortened Achilles tendons that are so common in women, or to high-heeled shoes, which increase the amount of dorsiflexion at the calcaneocuboid joint. We also observed that all the patients with long-delayed convalescence have been women — a point for which we can offer no explanation.

Discussion

The prolonged disability that so frequently occurs if treatment is delayed or neglected at the start deserves consideration. Adequate primary treatment requires complete avoidance of weight-bearing, as well as protection with elastic bandage or, preferably, a plaster boot for four to six weeks. If such treatment is neglected, the patients gradually develop typical, though mild, signs of a reflex neurocirculatory disturbance; slight cyanosis, coldness, edema, exaggerated pain and a shiny skin. These are the symptoms that persist for months. It seems possible, therefore, that this fracture lies at a "trigger point," and that by disregarding the original injury the patient continuously inflicts upon himself a series of minor painful stimuli that gradually build up severe causalgic pain. Thereafter the patient becomes extremely discouraged; he is invariably suspected of neurosis. Ultimate recovery seems virtually assured.

The question whether convalescence could be shortened by surgical removal of the chip fracture has often been raised. We believe that there is no indication for either early or late removal. In the early cases, simple immobilization and avoidance of weight-bearing assure a good result within a reasonable length of time. In the cases that have progressed to prolonged disability, surgery would only serve as a further insult to the reflex, neurocirculatory control. Sympathetic block might be helpful in this stage. We used it in only one case and obtained dramatic improvement. In the very late cases a triple arthrodesis is indicated.

Summary

A description of sprain-fractures of the anterior lip of the os calcis has been offered and two types of mechanism are suggested as causing them: compression through forcible dorsiflexion of the forefoot and periosteal avulsion through forcible stretching in equinovarus.

The diagnostic, clinical and roentgenographic characteristics of the injury have been presented and the importance of recognizing them early and giving adequate treatment has been emphasized.

The tendency to prolonged and complete disability in neglected cases has been pointed out, and a theory is offered to account for this.

References

1. Dachtler, H. W. Fracture of anterior superior portion of os calcis due to indirect violence. *Am. J. Roentgenol.* 25:629-631, 1931.
2. Christopher, F. Fracture of anterior process of calcaneus. *J. Bone & Joint Surg.* 13:877-879, 1931.
3. Gellman, M. Fractures of anterior process of calcaneus. *J. Bone & Joint Surg.* 33A:382-386, 1951.

CYCLIC PREMENSTRUAL CONGESTIVE HEART FAILURE*

MAX G. SHERER, M.D.,† AND WILLIAM E. R. GREER, M.D.‡

BOSTON

HEART FAILURE results when the heart is unable to respond with an increase in output sufficient to meet the demands of a person's daily activities. A cardiovascular system that is predisposed by disease may be thrown into failure in numerous ways. Abnormalities in fluid and electrolyte balance, resulting from excess salt intake,[1] impaired renal function and hormonal activity exerting a salt-retaining effect on the kidney,[2-5] play an important role in initiating and perpetuating congestive heart failure.

Premenstrual salt and water retention is common.[6-10] This results in cyclic gain and loss of weight with concomitant episodes of edema, bloating and distress, followed by intramenstrual diuresis with relief from these symptoms. The combination of heart disease and premenstrual fluid retention resulting in episodic congestive heart failure has heretofore received scant attention.[10, 11] Edeiken and Griffith,[12] in 1940, reported the first case of cyclic pulmonary edema with menses in mitral stenosis. In their case, serious pulmonary symptoms occurred in each of seventeen successive menstrual periods.

It is our purpose not only to report a second patient with cyclic pulmonary edema at the time of menses but, more importantly, to discuss the probable causative factors and mechanisms involved, in view of recent studies of adrenocortical activity.

CASE REPORT

R. R., a 37-year-old woman, was admitted to the Massachusetts Memorial Hospitals complaining of pain and fullness in the upper abdomen, shortness of breath and ankle swelling. The past history was noncontributory. There was no history suggestive of previous rheumatic fever. The patient had always experienced premenstrual distress. Nine and twelve years prior to admission the patient gave birth to two children; the pregnancies were normal. After the birth of her second child she had several "colds." She consulted a physician, who noted a heart murmur and advised against further pregnancies.

Four years prior to admission the patient noted sharp, constant nonradiating epigastric pain with bloating, shortness of breath and dependent edema commencing two to three days prior to her menstrual periods and ceasing four to five days thereafter. She was free of symptoms in the intermenstrual period. Her physician at this time noted "an irregular heart beat." Exclusion of fried and fatty foods and administration of digitalis afforded her some relief.

Three years prior to admission the patient's symptoms recurred more severely. They were again cyclic and were now accompanied by a marked increase in thirst and fluid intake in the premenstrual period. The previously noted premenstrual shortness of breath and ankle edema became more prominent. In addition, there was development of marked fatigue at these times. In spite of regularity of digitalis intake her condition steadily deteriorated, and she was advised by her physician to enter the hospital because of unsatisfactory progress on home care. The admission was just prior to her menstrual period.

Physical examination revealed a slightly obese, anxious woman. There was slight malar and periorbital edema. The lungs were clear, except for basilar rales heard posteriorly, which cleared after coughing. The heart was enlarged to the left in the fifth intercostal space 3 cm. beyond the midclavicular line. The rhythm was grossly irregular, and a systolic thrill was palpated at the base. Auscultation revealed double aortic and mitral murmurs of Grade II to III severity. A diastolic gallop was best heard near the apex. The liver was enlarged 4 to 5 cm. below the right costal margin and was firm, smooth and tender. There was + pitting edema of the sternum, legs and ankles and ++ edema of the sacrum. Blood pressure was 160/120, and there was a pulse deficit of 12 beats per minute.

Urine examination was negative. The remainder of the laboratory examination was not remarkable except for a circulation time of 30 seconds (arm to tongue) and a nonprotein nitrogen of 35 mg. per 100 cc.

An electrocardiogram revealed auricular fibrillation, ventricular premature beats and inverted T waves in all leads except V_5, which was diphasic.

The hospital course was uneventful. The patient responded well to a low-salt diet, mercurial diuretics and digitalis. She was discharged home on the sixth hospital day to return to the Cardiac Clinic at frequent intervals. The discharge diagnoses were: rheumatic heart disease, decompensation, auricular fibrillation and mitral stenosis; premenstrual fluid retention.

During the patient's course at the Cardiac Clinic she complained of continued epigastric distress and dyspnea. She was following the low-salt diet and was on daily digitoxin (0.1 mg.) plus 6 gm. of ammonium chloride daily. Physical examination revealed auricular fibrillation, enlargement of the heart and liver, ventricular premature beats and no edema. Her weight chart showed a 3-pound weight gain four days prior to the onset of her last period, followed by a weight loss of 4 pounds several days after menstruation started. She also noted frequency during this latter part of the period.

Thereafter, she was seen in the Cardiac Clinic at two-week intervals. Her course was one of progressive improvement. The auricular fibrillation, however, persisted in spite of one week of quinidine therapy. When she was last seen her complaints consisted solely of minimal evening ankle edema and mild menstrual cramps. The patient receives a mercurial diuretic just prior to each menstrual period.

DISCUSSION

The exchange of metabolites in vital organs is maintained by fluid volume adjustments of the vascular compartment. Renal activity, integrated by regulatory contributions of the cardiovascular system,[11] neurohypophysis,[13, 14] endocrine glands[8-10] and the nervous and humoral control of the blood pressure, plays a crucial role in the complex process. The control of the excretion of sodium chloride determines the volume of the extracellular fluids.[3] The anterior lobe of the pituitary gland releases ACTH in response to conditions of stress and nervous or humoral stimulation. In turn, the adrenal cortex secretes its steroids in response to ACTH.[13-16] Administration of 11-desoxycorticosterone (DOCA)

*From the Department of Medicine, Boston University School of Medicine and the Evans Memorial, Massachusetts Memorial Hospitals.

†Intern in medicine, Mount Sinai Hospital, New York City.

‡Instructor in medicine, Boston University School of Medicine; formerly, chief resident in medicine, Evans Memorial, Massachusetts Memorial Hospitals.

causes urinary retention of sodium and chloride and increased potassium excretion, with resultant increase in extracellular fluid volume.[8, 14] Congestive heart failure may be precipitated by administration of ACTH or DOCA in patients with diminished cardiac reserve[17, 18] because of the fluid-retaining properties of these agents.

The beginning and end of the menstrual cycle are characterized by a low titer of estrogenically active material.[7, 19, 20] Estrogen-oxidation products are present in large amounts during menstruation and the follicular phases of the cycle. At these periods pituitary gonadotrophic activity is maximal.[21-23] Estrogen-oxidation products have been demonstrated to have marked anterior-pituitary stimulating powers. Intact estrogens and unoxidized estrogen metabolites inhibit the hypophysis.[19, 24] Urinary pregnanediol excretion rises to a peak at about the middle of the luteal phase of the cycle but falls to very low levels a few days prior to the onset of bleeding.[7] Progesterone withdrawal following combined estrogen-progesterone administration results in increased excretion of estrogen-oxidation products, indicating progesterone inhibition of estrogen oxidation.[7, 20] Therefore the production of estrogen oxidation products is marked during the premenstrual phase, resulting in marked pituitary stimulation. Evidence for this is not lacking. Production of follicle-stimulating hormone, luteinizing hormone and prolactin increases before the onset of the menses.[19] Depression of serum diastase reflects increased adrenocortical activity secondary to ACTH release.[24, 25] Urinary excretion of antidiuretic substance at the time of menstruation has also been reported, suggesting posterior-pituitary stimulation.[12]

Large quantities of injected estrogens, testosterone and progesterone result in temporary sodium chloride and water retention, with resultant diuresis on withdrawal of these agents.[9-11] Premenstrual fluid and electrolyte retention is not due to these agents, since their titer is too low at the premenstrual phase of the cycle to cause the retention noted. The water and salt retention probably results from increased adrenocortical activity secondary to a rise in ACTH production caused by stimulation of the pituitary gland by estrogen-oxidation products.

In heart failure venous return is ample, but the work done by the heart is not adequate to meet the needs of the body. Increased fluid and electrolyte retention overtaxes an inadequate circulation, and heart failure is precipitated. Metabolic changes causing the retention of relatively small amounts of sodium chloride seem to play a decisive role in this regard.[1, 11, 26-28]

The case reported above presents an interesting combination of advanced rheumatic heart disease complicated by cyclic episodes of congestive heart failure induced by premenstrual fluid and electrolyte retention. Rheumatic heart disease is common during the childbearing age. No doubt many of these patients are subject to premenstrual fluid and electrolyte imbalances that aggravate their cardiac status but are unrecognized. The aim of therapy in cases such as this is to reduce bodily demand for a large volume of blood flow, to increase the effectiveness of systole and to combat the rise in blood volume and extracellular-fluid volume by withdrawing sodium or the influences promoting its retention. In this regard judicious restriction of salt intake and the administration of mercurial diuretics and cardiac glycosides are helpful. Hormone therapy may also be beneficial, especially in those cases complicated by menstrual headache, tension or irritability. Progesterone given daily for five days in doses of 25 mg., beginning six to eight days before the onset of menstruation, provides adequate supplementary therapy. This may be repeated for two or three cycles. Testosterone may be given to reduce pituitary activity. Depressant treatment with this agent, as a temporary measure in younger patients and for longer periods during the premenopausal climacteric, is consistently satisfactory. Methyl testosterone, 10 mg., is ingested daily, beginning on the fifth to tenth day of the cycle, until the onset of menstruation.[7, 8, 20]

Of further practical importance, it is recommended that elective operations be performed on female patients with rheumatic heart disease only during the middle of the intermenstrual phase of the cycle.

Summary

A case of rheumatic heart disease with cyclic episodes of congestive heart failure precipitated by premenstrual fluid and electrolyte retention is reported. The probable causative factors and operative mechanisms are discussed, with an outline of the possible therapeutic measures available for correction of the condition. Emphasis is laid on the need for being more aware of the condition because of the great number of women of childbearing age with advanced rheumatic heart disease.

References

1. Peters, J. P. Role of sodium in production of edema. *New Eng. J. Med.* 239:353-362, 1948.
2. Conn, J. W. Electrolyte composition of sweat; clinical implications as index of adrenal cortical function. *Arch. Int. Med.* 83:416-428, 1949.
3. Darrow, D. C., and Pratt, E. L. Fluid therapy: relation to tissue composition and expenditure of water and electrolyte. *J. A. M. A.* 143:365-373, 1950.
4. Forsham, P. H., Thorn, G. W., Prunty, F. T. G., and Hills, A. G. Clinical studies with pituitary adrenocorticotropin. *J. Clin. Endocrinol.* 8:15-66, 1948.
5. Friedberg, C. K. *Diseases of the Heart.* 1081 pp. Philadelphia and London: W. B. Saunders Company, 1949. P. 96.
6. Lippman, R. W. Nephrotic syndrome with exaggerated premenstrual water and salt retention. *Am. J. Med.* 8:686, 1950.
7. Smith, G. V. S. The ovaries. In *Textbook of Endocrinology.* Edited by Robert H. Williams. 793 pp. Philadelphia and London: W. B. Saunders Company, 1950. Pp. 349-449.
8. Thorn, G. W., and Emerson, K., Jr. Role of gonadal and adrenal cortical hormones in production of edema. *Ann. Int. Med.* 14: 757-769, 1940.
9. Thorn, G. W., and Engel, L. L. Effect of sex hormones on renal excretion of electrolytes. *J. Exper. Med.* 68:299-312, 1938.

10. Thorn, G. W., Nelson, K. R., and Thorn, D. W. Study of mechanism of edema associated with menstruation. *Endocrinology* **22**:155-163, 1938.
11. Dock, W. Congestive heart failure; adaptation of body to inadequate cardiac output. *J. A. M. A.* **140**:1135-1142, 1949.
12. Edeiken, J., and Griffith, J. Q., Jr. Cyclic pulmonary edema at menses in mitral stenosis: relief following irradiation of pituitary gland. *J. A. M. A.* **115**:287-289, 1940.
13. Hume, D. M. Role of hypothalamus in pituitary-adrenal cortical response to stress. *J. Clin. Investigation* **28**:790, 1949.
14. Thorn, G. W., et al. Studies on relation of pituitary-adrenal function to rheumatic disease. *New Eng. J. Med.* **241**:529-537, 1949.
15. Selye, H. Studies on adaptation. *Endocrinology* **21**:169-188, 1937.
16. *Idem.* General adaptation syndrome and diseases of adaptation. *J. Clin. Endocrinol.* **6**:117-230, 1946.
17. Massell, B. F., et al. Clinical response of rheumatic fever and acute carditis to ACTH. *New Eng. J. Med.* **242**:641-647 and 692-698, 1950.
18. Thorn, G. W., et al. Clinical usefulness of ACTH and cortisone. *New Eng. J. Med.* **242**:783-793, 824-834 and 865-872, 1950.
19. Smith, G. V. S., and Smith, O. W. Urinary excretion of estrogenic and gonadotropic hormones during menstrual cycles. Period of conception and early pregnancy. *New Eng. J. Med.* **215**:908-914, 1936.
20. Smith, O. W., Smith, G. V. S., and Schiller, S. Clinical experiments in relation to excretion of estrogens; urinary estrogens in normal menstrual cycle and in case of essential dysmenorrhea. *Am. J. Obst. & Gynec.* **45**:15-22, 1943.
21. Evans, H. M. Recent advances in our knowledge of anterior pituitary hormones. *Am. Scientist* **35**:465-484, 1947.
22. Smith, O. W. Pituitary responses of mature male rats to oxidative inactivation product of estrone. *Endocrinology* **35**:146-157, 1944.
23. *Idem.* Further studies on pituitary responses to oxidative inactivation product of estrone. *Proc. Soc. Exper. Biol. & Med.* **59**:242-246, 1945.
24. Smith, O. W., and Smith, G. V. S. Studies concerning cause and purpose of menstruation. *J. Clin. Endocrinol.* **6**:483-492, 1946.
25. Schiller, S., and Smith, O. W. Serum diastase and its relation to estrogen metabolism in pregnancy and menstrual cycle. *J. Clin. Endocrinol.* **3**:154-162, 1943.
26. Merrill, A. J. Edema and decreased renal blood flow in patients with chronic congestive heart failure: evidence of "forward failure" as primary cause of edema. *J. Clin. Investigation* **25**:389-400, 1946.
27. Reaser, P. B., and Burch, G. E. Radiosodium tracer studies in congestive heart failure. *Proc. Soc. Exper. Biol. & Med.* **63**:543-546, 1946.
28. Warren, J. V., and Stead, E. A., Jr. Fluid dynamics in chronic congestive failure: interpretation of mechanisms producing edema, increased plasma volume and elevated venous pressure in certain patients with prolonged congestive failure. *Arch. Int. Med.* **73**: 138-147, 1944.

Additional Reference

Heller, H., and Urban, F. F. Fate of antidiuretic principle of postpituitary extracts in vivo and in vitro. *J. Physiol.* **85**:502-518, 1935.

MEDICAL PROGRESS

PANCREATIC SURGERY (Concluded)*

Richard B. Cattell, M.D.,† and Kenneth W. Warren, M.D.‡

BOSTON

Surgical Treatment

Surgical procedures employed in chronic relapsing pancreatitis and pancreatolithiasis can be divided into those directed toward the pancreas, those indirectly affecting the pancreas and a combination of the direct and indirect procedures.

Indirect Methods

Biliary-Tract Operations

Cholecystectomy and choledochostomy. Gambill, Comfort and Bagenstoss[61] have emphasized the importance of eliminating pathologic conditions of the biliary tract, when present, in the management of the disease. They observed remissions of the disease of one to eight years' duration after cholecystectomy or cholecystectomy plus choledochostomy in approximately one third of the cases. Subsequent remissions were also observed after secondary choledochostomy with prolonged T-tube drainage.

Biliary diversion. In the presence of distention or obstruction of the biliary tract, a variety of diversional procedures are available and have been utilized. Cholecystojejunostomy and choledochojejunostomy, either in continuity or following transection of the common duct, accomplish biliary decompression and discourage or eliminate reflux of bile into the pancreatic ducts. Remissions have occurred after these procedures, but recurrences have likewise followed the remissions. One patient in our series obtained relief of symptoms and marked resolution of the pancreatic inflammation after division of the common duct with implantation into the duodenum. Bowers[73] has utilized choledochoduodenostomy with excellent results.

Sphincterotomy. Attempts to overcome biliary obstruction due to alleged spasm of the sphincter of Oddi, causing reflux of bile into the pancreas, have been vigorously pursued by Doubilet and Mulholland.[15-17] They have advocated transcholedochal sphincterotomy to eliminate the spastic sphincter and have reported, in several communications, their satisfactory experience with this maneuver. They have observed remission of symptoms, elimination of biliary-pancreatic reflux and increase in pancreatic enzymes in the duodenal contents in response to secretin administration, all after sphincterotomy. We have employed this procedure in a limited number of cases with some apparent success but with inconclusive results, and we plan to evaluate it further in selected cases. Its greatest appeal is its simplicity. We believe that it should be executed, when it is deemed applicable, by transduodenal approach rather than blindly through the common duct.

Operations on the Stomach

Chronic duodenal obstruction demands sidetracking of the gastric contents by either gastroenter-

*From the Department of Surgery, Lahey Clinic, Boston.

†Member, Department of Surgery, Lahey Clinic; staff member, New England Baptist Hospital; chief of surgical staff, New England Deaconess Hospital.

‡Member, Department of Surgery, Lahey Clinic; staff member, New England Deaconess and New England Baptist hospitals.

ostomy with or without pyloric exclusion or partial gastrectomy as advocated by Richman and Colp.[10, 11]

Chronic relapsing pancreatitis of sufficient severity to cause duodenal obstruction is not likely to respond to simple diversional gastroenterostomy, but this procedure may be necessary in the desperately ill patient or as an adjunct to some other type of operation. We have employed gastroenterostomy combined with vagotomy with moderate relief in one patient who had duodenal obstruction resulting from chronic relapsing pancreatitis.

Subtotal gastrectomy, according to Richman and Colp,[10, 11] accomplishes diversion of the gastric contents from the duodenum and thereby reduces the tendency to spasm of the sphincter, which might otherwise result from the contact of hydrochloric acid with the mucosa overlying the duodenal papilla. The absence of hydrochloric acid and food from the duodenum should reduce the formation of secretin and limit the functional response of the external secretion of the pancreas to the ingestion of food.

Johnson[77] reported failure in one case to obtain relief of pain from chronic pancreatitis after subtotal gastrectomy. We have observed 3 patients with chronic relapsing pancreatitis who have had partial gastrectomy without improvement in the course of chronic pancreatic disease, and we do not believe that partial gastrectomy should be done in this condition unless some specific disease in the stomach or duodenum warrants gastrectomy per se.

Interruption of Sympathetic Nerves

The control of chronic pancreatic pain by interruption of the sympathetic nerves is appealing because of the simplicity and relative safety of this method of attack. Since publication of the report of Marion,[78] Fontaine and his co-workers[79] and Mallet-Guy and his associates[14, 19, 80] in France, considerable interest in this approach to the therapy of chronic relapsing pancreatitis has been aroused in this country. Various aspects of this problem are considered in reports by deTakats and his associates,[81, 82] Smithwick,[83] Grimson and others,[84] Ray and Console,[85] Hurwitz and Gurwitz,[86] and Warren.[87] The enthusiastic report by Mallet-Guy and de Beaujeu,[19] who depend essentially on a left subdiaphragmatic splanchnicectomy in the application of this principle to the treatment of chronic relapsing pancreatitis, is difficult to reconcile with our own experience with interruption of sympathetic nerves. We have employed unilateral and bilateral thoracolumbar sympathectomy in this condition with varying results. Occasionally a patient has received dramatic relief from unilateral sympathectomy, and others have obtained moderate improvement with extensive bilateral interruption of the sympathetic nerves. Some have had no relief from bilateral sympathectomy. Even more disturbing to us has been the observation that in some patients the good results from this procedure were only temporary.

Rienhoff and Baker[88] have utilized combined radical sympathectomy and vagotomy in the treatment of chronic pancreatitis. Ray and Console,[85] on the other hand, have suggested that the operation on the sympathetic nervous system need not be so extensive as it is usually made.

The lack of standardization and the conflicting reports concerning the effectiveness of sympathetic-nerve surgery render proper appraisal of the procedure difficult, but in the present state of affairs relative to the therapy of chronic relapsing pancreatitis and pancreatolithiasis we prefer to regard the maneuver as an adjunct in reserve rather than a definitive procedure.

Direct Methods

Pancreatolithotomy. Simple pancreatolithotomy is occasionally feasible when a solitary calculus is blocking the periampullar portion of the duct of Wirsung. More commonly, of course, the stones are multiple and are so fused within arborizing segments of the ducts that they cannot be completely removed by transductal manipulation. If a solitary stone is removed one should be certain that the pancreatic component of the ampulla is patent. If obstruction is present the duct of Wirsung should be anastomosed to a loop of jejunum. When partial pancreatectomy is employed in the treatment of pancreatolithiasis residual stones should be removed, if possible, from the pancreatic remnant.

Ligation of the duct of Wirsung. Martin and Canseco[89] reported the ligation of the duct of Wirsung in the treatment of pancreatolithiasis. The operation performed by Rienhoff[22] consisted of preliminary removal of several small stones from the pancreatic ducts followed by ligation of the ducts by a series of transfixion ligatures. The patient was relieved of the pain. This procedure, to be effective, is based on the presence of functioning acinar tissue, which function we believe should be preserved if possible.

Pancreatojejunostomy. Cattell[90] has suggested the theoretical possibility of relieving the symptoms of pancreatolithiasis by anastomosis, in continuity, of the duct of Wirsung to a loop of jejunum. Bedrna and Sixie[70] (quoted by Kunc[71]) reported a case in which a hydropancreatic sac, which arose from obstruction of the duct of Wirsung by calculi, was anastomosed to the duodenum. The patient was symptom-free eighteen months later.

Wangensteen[91] has described a procedure utilized in his clinic in which the duct of Wirsung is transected near the ampulla of Vater and is in turn implanted into the jejunum. This procedure appears to be more difficult and more hazardous than anastomosis of the duct in continuity.

Distal pancreatectomy. Certain patients with chronic relapsing pancreatitis and with pancreato-

lithiasis are suitable candidates for distal pancreatectomy. Into this category will fall those patients who, after traumatic rupture of the pancreas, with division of the duct of Wirsung, develop stricture of the duct with chronic obstruction distal to the injury, with recurrent bouts of pancreatitis, cystic accumulations, persistent fistulas or progressive calcification. Even spontaneous recurrent pancreatitis or pancreatolithiasis may be confined to or involve particularly the distal segment of the gland. Mallet-Guy and associates[14] have reported 11 instances of distal pancreatectomy for chronic pancreatitis. We have utilized this procedure in 2 patients with pancreatolithiasis and in 3 with chronic relapsing pancreatitis. Two of the patients with chronic pancreatitis without stones had had previous serious injury to the pancreas. The results of distal pancreatectomy have been good in all patients without stones and in one patient with pancreatolithiasis. The condition of one patient with diffuse calcification of the pancreas was improved but not relieved by distal pancreatectomy, and a right-thoracolumbar sympathectomy was subsequently performed, with further improvement.

The choice of distal pancreatectomy should be made with care, since chronic relapsing pancreatitis and, more particularly, pancreatolithiasis usually indicate obstruction of the duct of Wirsung near the ampulla; distal pancreatectomy will not relieve this obstruction.

Pancreatoduodenectomy. We have observed a type of chronic relapsing pancreatitis, with and without stones, in which there are multiple areas of intrapancreatic obstruction with marked fibrosis and multiple cystic areas in which it appears that no procedure short of proximal pancreatectomy would offer a reasonable prospect of relief to the patient. Despite the obvious technical difficulties involved in resecting the duodenum and head of the pancreas under these circumstances, this risk must frequently be assumed. We have selected this procedure in 9 cases. In 7, pancreatolithiasis was present. In all but 2, one or more previous surgical procedures had failed to relieve the symptoms of the disease. There were no postoperative deaths, although one of the patients who was considerably improved died eighteen months later from chronic alcoholism and malnutrition. Pancreatoduodenectomy has given the best results to date of any of the procedures we have employed in chronic relapsing pancreatitis and pancreatolithiasis. In advocating this maneuver, as in electing it at the time of abdominal exploration, one should not lose sight of the fact that the condition to which it is being applied is benign and that the technical hazards of pancreatoduodenectomy in the presence of chronic relapsing pancreatitis or pancreatolithiasis are greater than they are when the operation is being performed for carcinoma of the pancreas or ampulla of Vater.

Total pancreatectomy. Whipple[92] and Waugh, Rhoads and Clagett[93] have employed total pancreatectomy for chronic relapsing pancreatitis and pancreatolithiasis. There were 2 postoperative deaths in 5 patients, and one survivor died three months later from an overdose of insulin. Thus, the mortality of the procedure has been too high to justify its application as a primary operation for this disease. The removal of the entire pancreatic remnant after failure of partial pancreatectomy to relieve the symptoms of chronic relapsing pancreatitis or pancreatolithiasis should be considered when less hazardous therapeutic measures offer no real prospect of relief.

Trauma

Pancreatic Injuries and Fistulas

Injuries to the pancreas are not common, but the consequences of such an injury are frequently grave. Wright, Prigot and Hill[94] reported several cases of traumatic subcutaneous injuries to the pancreas and emphasized that these injuries can result from trivial trauma, that the symptoms of pancreatic injury may be delayed for hours or a few days, that the presence of pancreatic involvement is frequently overlooked and that determinations of serum-amylase values after upper-abdominal trauma should be routine. Kipen[97] has reported an instance of pancreatic calculosis following trauma, indicating that chronic pancreatitis can result from such an injury. Warren[97] has recently reviewed the experiences of the Lahey Clinic with traumatic and operative injuries to the pancreas and has pointed out the complications that may result from pancreatic injury. These complications include acute pancreatic edema and necrosis, immediate or delayed massive hemorrhage, pancreatic cysts, pancreatic abscess, diabetes mellitus, steatorrhea, internal and external pancreatic fistula, subdiaphragmatic abscess and pancreatic calcification.

The immediate care of violent traumatic injuries to the pancreas should be limited to the control of hemorrhage, the evacuation of hematomas and adequate drainage of the areas of injury. If a temporary fistula ensues, the skin should be protected from erosion by simple suction or sump drainage. Persistent fistulas are preferably treated by distal pancreatectomy if the site of origin involves the body or tail of the gland. Persistent fistulas arising from the ampullary portion of the duct of Wirsung should be treated by anastomosing the duct to a loop of jejunum. Attempts to eliminate these stubborn fistulas by injecting sclerosing agents, by the utilization of radium or x-ray therapy or by the implantation of the fistulous tract in a segment of the upper gastrointestinal tract are not likely to succeed.

Operative Injuries

Injuries to the distal extremity of the pancreas during operations on the cardiac portion of the

stomach, spleen or left kidney are usually not serious if recognized and treated at the time of the original operation. If the tail of the pancreas is amputated, the divided end should be closed with mattress sutures of silk and the area adequately drained.

Millbourn[20] has considered the problem of pancreatic affections following subtotal gastrectomy, and Warren[95] has related the experience of the Lahey Clinic with the pancreatic complications of gastric surgery. Methods of avoiding pancreatic injuries in the course of surgical procedures on the stomach have been reviewed, and the appropriate methods of immediate and delayed repair of these injuries have been described.

Tumors

Islet-Cell Tumors and Hyperinsulinism

Although no dramatic progress has been made during the last three years in the recognition and treatment of islet-cell tumors and hyperinsulinism, some worth-while papers relating to various aspects of this problem have appeared. Howard, Moss and Rhoads[98] collected 398 cases of islet-cell tumor and hyperinsulinism from the literature. They found that these tumors, although slightly more common in the body and tail, were fairly evenly distributed throughout the pancreas. Multiple tumors occurred in approximately 12.6 per cent of cases. Seven islet-cell tumors have been found in ectopic pancreatic masses. In 118 cases a tumor could not be located during the original surgical exploration. Thirty-seven of these patients were eventually found to have an islet-cell tumor. In 12 of the 37, an islet-cell tumor was removed by subtotal pancreatectomy without identification of the tumor at the time of exploration, in 12 others the tumor was removed at a subsequent operation and in 13 instances the tumor was discovered at autopsy. In 81 patients an islet-cell tumor was not demonstrated. Partial pancreatectomy was performed in 56 of these, with satisfactory response in 46.4 per cent.

The enigma of the suspectedly malignant adenoma of the pancreas has not been resolved. According to Howard, Moss and Rhoads,[98] only one of 36 survivors among 41 patients operated on for a suspectedly malignant adenoma was thought to have subsequent metastases, and this patient was alive nine years after subtotal pancreatectomy.

These authors found no case of five-year salvage in obviously malignant tumors of the islet cells. Very few such tumors have been resected. In assessing these data one should bear in mind that some of the islet-cell tumors that have been regarded only with suspicion may well have been malignant and that therefore some malignant lesions may have been completely eradicated.

Brown, Neville and Hazard[97] reported an interesting case in which a large islet-cell adenoma arising in the head of the pancreas caused symptoms of duodenal obstruction without hypoglycemia. The tumor measured 7.5 cm. at its greatest diameter.

Perkins, Desforges and Guttas[96] have considered anew the differentiation of hyperinsulinism from functional hypoglycemia and have concluded that there is no single criterion for differentiating the two, that fasting blood-sugar determinations are more valuable than tolerance tests and that a history of progressive increase in the frequency and the severity of the attacks is a valuable guide to the presence of organic hyperinsulinism. Willner and Weinstein[99] have reported a case of islet-cell adenoma with increased insulin secretion in the urine.

Crain and Thorn[100] have proposed two tests for exclusion of disease of the pituitary and adrenal glands in the differential diagnosis of hypoglycemia. The first consists of observing the eosinophilic response to the injection of epinephrine. The epinephrine stimulates the pituitary gland to secrete ACTH, which in turn depresses the eosinophil count. If a normal fall of 50 per cent in circulating eosinophils occurs, one may eliminate from consideration serious disease of the pituitary or adrenal cortex. The second test consists of injecting ACTH directly and measuring the eosinophils. A similar depression indicates an intact adrenal cortex.

New medical attempts to eliminate hyperinsulinism have been made. Talbot, Crawford and Bailey[101] reported a moderate response to alloxan in one case, but the end result was not good. The severe, toxic side-effects of this drug preclude its use at the present time. McQuarrie and associates[102] employed ACTH in 5 children with hypoglycemia of undetermined etiology. All 5 patients were relieved of their hypoglycemic symptoms during the administration of the hormone. One patient was maintained for one month on a dosage of 18 mg. every two days and on 10 to 15 mg. every two days thereafter for more than five months. This preparation may have a place in the therapy of hypoglycemia in those patients in whom no adenoma is found at surgical exploration or in those cases in which subtotal pancreatectomy has failed to eliminate the attacks of hypoglycemia.

Pancreatic Cysts

The lack of consistency in the choice of surgical methods of dealing with pancreatic cysts continues to characterize the literature relative to this subject. For many years the principle of marsupialization was applied rather indiscriminately to almost all pancreatic cysts. Today there is a growing tendency to apply, with an equal lack of discernment, the principle of internal drainage to a large percentage of pancreatic cysts. Carter and Slattery[103] reported a case in which a cyst was anastomosed to an accidental rent in the common duct. Meyer, Sheridan and Murphy[104] utilized cystocholecystostomy in 4 cases and cystojejunostomy in 2. Kunc,[71]

Paul,[105] and Brandenburg, Maddock and Schweitzer [106] have reported satisfactory response to transgastric cystogastrostomy.

Although the internal drainage of pancreatic cysts has a limited application in the management of the disease, it should not, in our opinion, become a common method of treatment. Meyer and others[104] reported 2 deaths in patients treated by cystojejunostomy, and in 2 of 4 cases treated by cystocholecystostomy the same authors found that a residual cyst persisted. Maxeiner and Maxeiner[107] recorded a case in which cystogastrostomy was performed on a pseudocyst that appeared after an attack of acute pancreatitis. Beginning on the sixth postoperative day, the patient had the first of a series of massive gastric hemorrhages, requiring 60 transfusions in 120 days. Subtotal gastrectomy was performed and a peptic ulcer was found at the site of the cystogastrostomy. We have observed 2 patients at the clinic within the past two years who had persistent or recurrent cysts following internal drainage procedures performed elsewhere.[66]

Jemerin and Samuels[108] published in 1948 an excellent review of the subject of cystadenoma of the pancreas and described the successful removal of a large cystadenoma of the head of the pancreas that compressed but did not obstruct the common bile duct, the portal vein and the hepatic artery. Herrman and Asbell,[109] in 1949, reported 2 cases of cystadenoma of the pancreas.

Warren,[110] in 1948, reported 16 cases of pancreatic cysts observed at the Lahey Clinic, and indicated a preference for individualization in the choice of therapeutic measures in dealing with these problems.

Carcinoma of the Pancreas, Ampulla of Vater and Periampullar Structures

Diagnosis. The difficulty in the clinical detection of carcinoma of the pancreas and the ampulla of Vater has been considered by many authors. Child[116] has again pointed out these difficulties and has summarized the various views of many men who have had considerable experience with this problem. Silver and Lubliner[111] analyzed 104 cases and reiterated the observation that weight loss, pain and anorexia are the earliest signs of cancer of the pancreas and that jaundice appears less frequently and later than these initial symptoms. Painless jaundice, associated with a palpable gall bladder, occurred in less than 25 per cent of cases of carcinoma of the head of the pancreas and the ampulla of Vater observed at this clinic.

Attempts to distinguish by clinical means between carcinoma arising in the head of the pancreas and carcinoma of the ampulla of Vater should be encouraged. Ross and Klinge[112] found that pain was associated with carcinoma of the head of the pancreas in 25 of 30 cases but pain was absent in 8 of 10 cases of carcinoma of the ampulla of Vater. Even more significantly, the pain consistently preceded the jaundice in the presence of carcinoma of the pancreas. Finally, these authors observed that whereas all patients with carcinoma of the ampulla of Vater had jaundice, 20 per cent of patients with carcinoma of the head of the pancreas did not have jaundice. Cattell[113] has emphasized in this regard that carcinoma arising in the head of the pancreas is characterized by pain, fatigue, loss of weight, and bowel symptoms prior to the onset of jaundice, whereas in carcinoma of the ampulla of Vater the jaundice precedes the onset of other symptoms. Furthermore, he has stressed that carcinoma arising in the head of the pancreas gives rise to early obstruction of the duct of Wirsung, leading to digestive manifestations characteristic of external pancreatic deficiency.

McNeer and Ewing[114] demonstrated the presence of malignant cells by a study of material obtained through duodenal drainage in a patient with jaundice. At operation an adenocarcinoma arising from pancreatic ductal tissue was found. In another patient the diagnosis of carcinoma was made by the cytologic analysis of bile obtained from a T tube that had been inserted at a previous operation at which a carcinoma of the head of the pancreas was overlooked. Lemon and Byrnes[115] utilized the cytologic analysis of aspirated duodenal contents in the study of patients with carcinoma of the liver, pancreas or biliary tract. Cancer was diagnosed or suspected in 11 cases by this method.

The importance of performing an exploratory operation on all patients with obstructive jaundice and, indeed, on all patients with jaundice except those with unequivocal evidence of primary hepatocellular disease is emphasized by Child.[116]

Diagnosis at the operating table of carcinoma of the pancreas or ampullar region. That the diagnosis of carcinoma of the pancreas, even with the abdomen open, is frequently difficult is reflected in the recent communications by Child,[116] Carlson,[117] Probstein and associates[118] and Cattell.[119, 120] Jaundice associated with distention of the extrahepatic biliary tract may result from an impacted common-duct stone, chronic pancreatitis or carcinoma in the head of the pancreas or ampullar region. The difficulty of assessing an indurated pancreatic mass cannot always be readily resolved. The limitations of conventional means of biopsy are great and the hazards of such a procedure, in terms of invitation to serious hemorrhage or pancreatic fistula, are considerable. It is the consensus today that such biopsies are generally futile and are not worth the risks involved. Kirtland,[121] in evaluating this aspect of the diagnosis of carcinome of the pancreas, found 77 cases in which an erroneous diagnosis of carcinoma of the head of the pancreas was made at operation. Nine of these patients were subjected to radical pancreatoduodenectomy. Kirtland[121] has proposed that multiple biopsies of suspicious areas of the pancreas

be taken with the Vim-Silverman needle in order to reduce this incidence of error to a minimum. Cattell[120] has been reluctant to accept the diagnosis of carcinoma of the head of the pancreas or ampulla of Vater in the absence of dilatation of the common bile duct or obstruction of the duct of Wirsung. An obstructed duct of Wirsung is not difficult to find if the surface of the pancreas is palpated longitudinally at the junction of the upper and middle thirds of the organ. Dilatation of this structure, from which pancreatic fluid may be obtained by aspiration, is perhaps the most reliable single sign of carcinoma of the head of the pancreas or ampulla of Vater. Frozen-section analysis of adjacent lymph nodes, when positive for cancer cells, will be decisive in establishing the diagnosis of carcinoma of the pancreas.

Determination of operability in carcinoma of the head of the pancreas. Cattell[120] has emphasized that it is possible to determine the operability of a malignant lesion arising in the head of the pancreas or ampulla of Vater without the preliminary division of the gastrointestinal, biliary or pancreatic tract. By dividing the right extremity of the gastrocolic omentum one may demonstrate the freedom or involvement of the superior mesenteric vessels, and by dividing the right gastric and gastroduodenal arteries one may expose the superior segment of the portal vein without making resection mandatory.

The demonstration of distant metastases, local spread beyond the possible limit of resection, involvement of the superior mesenteric vessels or involvement of the portal vein contraindicates resection.

Rate of operability. Child,[116] in an analysis of 125 cases of carcinoma of the head of the pancreas observed at the New York Hospital from 1935 to 1945, found that the tumor could be removed in only 23 cases. Cattell and Pyrtek[72] reported from this clinic that 56 of 165 patients (34 per cent) with carcinoma of the head of the pancreas or ampulla of Vater who were operated on between 1942 and 1948 had radical pancreatoduodenal resections. Priestley, Walters, Gray and Waugh[122] reported that resection of the pancreas for carcinoma was performed in only 5.7 per cent of cases of pancreatic carcinoma observed at the Mayo Clinic in 1949. These low rates of resectability, as compared with resectability rates for malignant lesions in other segments of the gastrointestinal tract, indicate the urgency of earlier diagnosis of carcinoma of the pancreas.

Type of Gastrointestinal Reconstruction Following Pancreatoduodenectomy

Although the precise manner of reconstruction of the gastrointestinal tract following radical pancreatoduodenal resection is to some extent a matter of personal preference, certain principles have proved valid and should be observed. The pancreatic remnant should be anastomosed to the jejunum either by direct anastomosis or by means of a necrosing suture as advocated by Cattell.[120] Further evidence that such anastomoses remain functional has been advanced by Reynolds and Pearse[123] and by Child.[116] We believe that direct mucosa-to-mucosa suture of the duct to the jejunum is preferable, even when the duct of Wirsung is not dilated. Several principles referable to the manner of restoring the biliary flow into the intestine now seem obvious. In the one-stage procedure, it is preferable to anastomose the divided common duct to the jejunum rather than to employ cholecystojejunostomy. Care must be taken, in this regard, not to occlude the cystic duct in the process of uniting the common duct to the intestine. If the cystic duct is encroached on, the gall bladder should be removed. If in the election of a two-stage procedure a cholecystojejunostomy has been performed at the first operation, at the second procedure either the common duct should be anastomosed to the jejunum or the divided end should be carefully inverted rather than occluded by simple ligature. The preference for the use of a jejunal loop or the Roux Y procedure is largely individual. The important point, in this respect, is to ensure that the stoma between the biliary tract and the jejunum is of sufficient size to avoid secondary stricture. It is generally thought today that recurrent cholangitis following anastomotic procedures for biliary decompression results from stricture of the stoma rather than from reflux of gastrointestinal contents into the biliary tree.

Despite the recommendation of Pearse[124] in 1946, little progress has been made in standardizing the manner of reconstruction of the gastrointestinal tract following pancreatoduodenectomy.

Some attention has been given to the consideration of jejunal ulceration following resection of the duodenum and head of the pancreas, and Orr[125] has stressed the importance of placing the gastrojejunal anastomosis distal to the biliary and pancreatic anastomoses. We know of no instance of jejunal ulceration following pancreatoduodenectomy for carcinoma at the clinic, but one patient who had a pyloric exclusion for chronic relapsing pancreatitis had a perforated jejunal ulcer eighteen months after operation despite the fact that the gastrojejunostomy was distal to the entrance of bile and pancreatic secretion into the intestine.

Appraisal of Pancreatoduodenal Resection for Carcinoma of the Pancreas

A few large series of cases of pancreatoduodenectomy have been reported by Whipple,[126] Orr,[125] Waugh,[127] Bartlett,[128] Cattell and Pyrtek,[72] and Child.[116] Only isolated instances of five-year survival after resection for carcinoma arising in the head of the pancreas have been reported.

Cattell and Pyrtek,[72] in 1949, recorded follow-up studies on a group of 56 patients who had had pancreatoduodenal resection for malignant lesions involving the head of the pancreas, the ampulla of Vater, the duodenum and the distal end of the common bile duct. This series included 20 tumors that arose in the ampulla of Vater, 30 in the head of the pancreas, 4 in the duodenum and 2 in the common duct.

Only 12 of the 48 survivors had been operated on prior to 1944 and were thus suitable material for application of the conventional five-year measure of survival. Three of the 12 (25 per cent), each of whom had carcinoma of the ampulla of Vater, were living and well more than five years after operation, and 6 of the original 12 (50 per cent) lived three years or more.

Of 25 patients who survived pancreatoduodenectomy for carcinoma of the head of the pancreas, 18 died of recurrence after an average survival span of eleven months. The longest duration of life was nineteen months. In the 7 patients who were still living at the time of the survey the longest period of survival was forty-one months.

It seems reasonable to conclude that pancreatoduodenal resection for carcinoma of the ampulla of Vater is a valid procedure, in terms of both maintaining a low operative mortality and achieving an acceptable degree of long-term salvage. Unfortunately, the results following resection for carcinoma arising in the head of the pancreas are poor.

Mortality

Child[116] collected a total of 194 cases of radical pancreatoduodenectomy in which there were 51 postoperative deaths, a mortality of 26.2 per cent. Brunschwig[129] reported, in 1947, 11 consecutive resections with one death (11 per cent). Cattell and Warren[25] recorded a mortality of 14 per cent in 56 resections. In the last 41 pancreatoduodenal resections performed at the clinic there were 3 deaths, a mortality of 7.3 per cent. Miller, Dockerty, Wollaeger and Waugh[120] recently reported a mortality of 29.6 per cent for carcinoma of the head of the pancreas and 11.8 per cent for carcinoma of the papilla. Thus it is obvious that the procedure can be performed with a reasonable mortality under favorable circumstances.

Total Pancreatectomy

The diffuse involvement of the pancreas in certain benign and malignant diseases has been responsible for the employment of total pancreatectomy in a limited number of cases. The operative mortality of the procedure, as recently determined by Warren[121] in a review of 17 cases of carcinoma, was 53 per cent, and the longest salvage period was approximately fourteen months. During the same period 7 cases of total pancreatectomy for benign lesions were collected, showing an operative mortality of 28.6 per cent. The composite mortality rate in 24 cases was 45.8 per cent. Instances of total pancreatectomy have been recorded recently by Gaston,[122] Jarrin,[123] Bowers,[124] Rhoads and others,[125] Waugh,[93] Warren[121] and Fallis and Szilagyi.[126] The first successful total pancreatectomy was performed in 1944 for removal of a nonpalpable islet-cell adenoma. The patient was alive and well six years after the operation. Fallis, also in 1944, executed the first successful total pancreatectomy for a malignant lesion. The patient survived fourteen months. The first total extirpation of the pancreas for chronic pancreatitis associated with diffuse calcification of the organ was credited to Clagett.[93] This patient died at home about three months later as the result of an unrecognized hypoglycemic reaction. The hope that radical extension of the scope of resection in malignant lesions of the pancreas would improve the prospects for cure or long-term salvage has not as yet materialized. Pessimism in this regard should be curbed to the extent that total pancreatectomy, as it has been employed in the past in the management of carcinoma of the pancreas, has been applied almost exclusively to far advanced lesions.

Summary

Rapid progress in pancreatic surgery is indicated by more frequent diagnoses, better selection of proposed surgical procedures and lower mortality. The work reported in pertinent papers during the past three years has been reviewed and discussed in the light of the authors' experience.

References

77. Johnson, W. M. Subtotal gastrectomy in treatment of chronic recurrent pancreatitis. *Gastroenterology* **14**:590, 1950.
78. Marion, P. Sur le traitement des pancréatites aiguës par les infiltrations splanchniques. *Lyon chir.* **40**:315-324, 1945.
79. Fontaine, R., Forster, E., and Stefanini, C. Résultats éloignés de 63 splanchnicectomies pour diverses affections (en dehors de l'hypertension artérielle chronique permanente). *Lyon chir.* **41**:279-300, 1946.
80. Mallet-Guy, P., and Lacour, R. Indications et résultats de la pancréatectomie gauche; d'après 16 observations personnelles. *Lyon chir.* **44**:169-184, 1949.
81. deTakats, G., and Walter, L. E. Treatment of pancreatic pain by splanchnic nerve section. *Surg., Gynec. & Obst.* **85**:742-746, 1947.
82. deTakats, G., Walter, L. E., and Lasner, J. Splanchnic nerve section for pancreatic pain; second report. *Ann. Surg.* **131**:44-57, 1950.
83. Smithwick, R. H. Discussion. *Ann. Surg.* **124**:1008, 1946.
84. Grimson, K. S., Hesser, F. H., and Kitchin, W. W. Early clinical results of transabdominal celiac and superior mesenteric ganglionectomy, vagotomy, or transthoracic splanchnicectomy in patients with chronic abdominal visceral pain. *Surgery* **22**:230-238, 1947.
85. Ray, B. S., and Console, A. D. Relief of pain in chronic (calcareous) pancreatitis by sympathectomy. *Surg., Gynec. & Obst.* **89**:1-8, 1949.
86. Hurwitz, A., and Gurwitz, J. Relief of pain in chronic relapsing pancreatitis by unilateral sympathectomy. *Arch. Surg.* **61**: 372-378, 1950.
87. Warren, K. W. Management of pancreatic injuries. *S. Clin. North America* **31**:789-802, 1951.
88. Rienhoff, W. F., Jr., and Baker, B. M. Pancreolithiasis and chronic pancreatitis; preliminary report of case of apparently successful treatment by transthoracic sympathectomy and vagectomy. *J. A. M. A.* **134**:20, 1947.
89. Martin, L., and Canseco, J. D. Pancreatic calculosis. *J. A. M. A.* **135**:1055-1060, 1947.
90. Cattell, R. B. Discussion. *Ann. Surg.* **124**:1006, 1946.
91. Wangensteen, O. H. Discussion. *Ann. Surg.* **132**:797, 1950.

92. Whipple, A. O. Radical surgery for certain cases of pancreatic fibrosis associated with calcareous deposits. *Ann. Surg.* **124**: 991-1008, 1946.

93. Waugh, J. M., et al. Total pancreatectomy; symposium presenting 4 successful cases and report on metabolic observations. *Proc. Staff Meet., Mayo Clin.* **21**:25-46, 1946.

94. Wright, L. T., Prigot, A., and Hill, L. M. Traumatic subcutaneous injuries to pancreas. *Am. J. Surg.* **80**:170-175, 1950.

95. Warren, K. W. Acute pancreatitis and pancreatic injuries following subtotal gastrectomy. *Surgery* (in press).

96. Howard, J. M., Moss, N. H., and Rhoads, J. E. Hyperinsulinism and islet cell tumors of the pancreas; with 398 recorded tumors. *Internat. Abstr. Surg.* **90**:417-455, 1950.

97. Brown, C. H., Neville, W. E., and Hazard, J. B. Islet-cell adenoma, without hypoglycemia, causing duodenal obstruction. *Surgery* **27**:616-620, 1950.

98. Perkins, H. A., Desforges, J. F., and Guttas, C. G. Adenoma of islands of Langerhans; its differentiation from functional hypoglycemia. *New Eng. J. Med.* **243**:281-285, 1950.

99. Willner, V., and Weinstein, V. A. Islet cell adenoma of pancreas with increased insulin excretion in urine. *New York State Med. J.* **50**:1103-1106, 1950.

100. Crain, E. L., Jr., and Thorn, G. W. Functioning pancreatic islet cell adenomas; review of literature and presentation of two new differential tests. *Medicine* **28**:427-447, 1949.

101. Talbot, N. B., Crawford, J. D., and Bailey, C. C. Use of mesoxalyl urea (alloxan) in treatment of infant with convulsions due to idiopathic hypoglycemia. *Pediatrics* **1**:337-345, 1948.

102. McQuarrie, I., Bauer, E. G., Ziegler, M. R., and Wright, W. S. Metabolic and clinical effects of pituitary adrenocorticotrophic hormone in spontaneous hypoglycemosis. *Proceedings of First Clinical ACTH Conference.* Edited by John R. Mote. 607 pp. Philadelphia: The Blakiston Co., 1950. Pp. 225-240.

103. Carter, R. F., and Slattery, L. Cystadenomata of pancreas; surgical report. *Am. J. Digest Dis.* **3**:705-707, 1936.

104. Meyer, K. A., Sheridan, A. I., and Murphy, R. F. Pseudocysts of pancreas; report of 31 cases. *Surg., Gynec. & Obst.* **88**:219-229, 1949.

105. Paul, M. Pancreatic cysts. *Brit. J. Surg.* **37**:99-104, 1949.

106. Brandenburg, F. H., Maddock, S. J., and Schweitzer, R. J. Personal communication.

107. Maxeiner, S. R., Jr., and Maxeiner, S. R. Pancreatic cystgastrostomy; discussion and report of case. *Surgery* **27**:919-921, 1950.

108. Jemerin, E. E., and Samuels, N. A. Cystadenoma of pancreas. *Ann. Surg.* **127**:158-170, 1948.

109. Herrman, C. S., and Asbell, N. Cystadenoma of pancreas. *Am. J. Surg.* **78**:107-112, 1949.

110. Warren, K. W. Pancreatic cysts. *S. Clin. North America* **28**:753-760, 1948.

111. Silver, G. B., and Lubliner, R. K. Carcinoma of pancreas; clinicopathologic survey. *Surg., Gynec. & Obst.* **86**:703-716, 1948.

112. Ross, C. A., and Klinge, F. W. Pain and hyperamylasemia as early signs of carcinoma of head of pancreas and ampulla of Vater. *Gastroenterology* **12**:204-208, 1949.

113. Cattell, R. B. Anastomosis of duct of Wirsung; its use in palliative operations for cancer of head of pancreas. *S. Clin. North America* **27**:636-643, 1947.

114. McNeer, G., and Ewing, J. H. Exfoliated pancreatic cancer cells in duodenal drainage: case report. *Cancer* **2**:643-645, 1949.

115. Lemon, H. M., and Byrnes, W. W. Cancer of biliary tract and pancreas; diagnosis from cytology of duodenal aspirations. *J. A. M. A.* **141**:254-257, 1949.

116. Child, C. G., III. Advances in management of pancreaticoduodenal cancers. In *Advances in Surgery*, Vol. 2. 190 pp. New York: Interscience Publishers, Inc., 1949. Pp. 495-561.

117. Carlson, R. I. Problem of diagnosis at time of operation in tumors of head of pancreas. *Surgery* **28**:672-679, 1950.

118. Probstein, J. G., Sachar, L. A., and Rindskopf, W. Biopsies of pancreatic masses. *Surgery* **27**:356-359, 1950.

119. Cattell, R. B. Resection of pancreas; discussion of special problems. *S. Clin. North America* **28**:753-766, 1943.

120. *Idem.* Technic for pancreatoduodenal resection. *S. Clin. North America* **28**:761-775, 1948.

121. Kirtland, H. B., Jr. Safe method of pancreatic biopsy. *Am. J. Surg.* (in press).

122. Priestley, J. T., Walters, W., Gray, H. K., and Waugh, J. M. Annual report on surgery of biliary system and pancreas for 1949. *Proc. Staff Meet., Mayo Clin.* **25**:685-692, 1950.

123. Reynolds, J. T., and Pearse, H. E. Radical pancreaticoduodenectomy; report of two cases of proved successful implantation of pancreatic duct into jejunum. *Surgery* **25**:815-823, 1949.

124. Pearse, H. E. Should we standardize reconstruction after pancreaticoduodenectomy? *Surgery* **20**:663-669, 1946.

125. Orr, T. G. Pancreaticoduodenectomy for carcinoma of ampulla and ampullary region. *Surgery* **18**:144-158, 1945.

126. Whipple, A. O. Observations on radical surgery for lesions of pancreas. *Surg., Gynec. & Obst.* **82**:623-631, 1946.

127. Waugh, J. M. Radical resection of head of pancreas and total pancreatectomy. *J. A. M. A.* **137**:141-144, 1948.

128. Bartlett, M. K. Status of pancreaticoduodenal resection. *S. Clin. North America* **27**:1032-1036, 1947.

129. Brunschwig, A. One-stage pancreatoduodenectomy. *Surg., Gynec. & Obst.* **88**:161-164, 1947.

130. Miller, E. M., Dockerty, M. B., Wollaeger, E. E., and Waugh, J. M. Carcinoma in region of papilla of Vater; study of cases in which resection was performed. *Surg., Gynec. & Obst.* **92**:172-182, 1951.

131. Warren, K. W. Some aspects of total pancreatectomy. *Lahey Clin. Bull.* **7**:86-96, 1951.

132. Gaston, E. A. Total pancreatectomy. *New Eng. J. Med.* **238**:345-354, 1948.

133. Jarrin, N. Case of total pancreatectomy. In *Alexander W. Blain Birthday Tribute.* 128 pp. March 4, 1950. Pp. 68-72.

134. Bowers, R. F. Surgical procedures for pancreatic lesions: review of pancreatic surgery. *Arch. Surg.* **60**:817-836, 1950.

135. Rhoads, J. E., Howard, J. M., and Moss, N. H. Clinical experiences with surgical lesions of pancreas. *S. Clin. North America* **29**: 1801-1816, 1949.

136. Fallis, L. S., and Szilagyi, D. E. Observations on some metabolic changes after total pancreatoduodenectomy. *Ann. Surg.* **129**: 639-667, 1948.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

BENJAMIN CASTLEMAN, M.D., *Associate Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 37261

PRESENTATION OF CASE

A fifty-seven-year-old man was admitted to the hospital because of a persistent productive cough.

Approximately four months prior to admission the patient "caught a cold" and developed a persistent severe cough that produced whitish sputum. Three and a half months before entry, because the cold did not clear, he consulted a physician, who had x-ray films of the chest taken and told the patient that he had pneumonia and fluid in the left chest. Three sputum samples and clear straw-colored chest fluid recovered by thoracentesis were reported by the State laboratory as negative for tubercle bacilli by smear, culture and guinea-pig inoculation. The patient was given penicillin for eleven days without significant relief of the symptoms. He was also given iron and vitamins. During the entire illness he remained in bed at home, with his temperature ranging between 99.5 and 100°F. He had anorexia and lost 12 to 14 pounds in weight. The sputum was at first whitish and later yellow; during the few weeks prior to entry it was blood-tinged. The patient raised as much as a half pint daily on occasions, although there were periods when the cough was nonproductive. He also noted occasional dull nonradiating anterior chest pain that was usually brought on by coughing. About six weeks after the onset of the symptoms he felt somewhat better but was too weak to get out of bed. One month before admission he noted a nontender lump in the left breast that did not increase in size. Shortly after this he noted the onset of right-lower-quadrant postprandial discomfort. For the week prior to admission the ankles were swollen; at about the same time the patient had grippe, with a temperature of 102°F. and worsening of his cough. The bowel movements had been regular, but the stools were black during the period of taking iron pills. The patient had not noted any night sweats, chills, dyspnea, diarrhea, bloody stools or jaundice.

The patient had always enjoyed excellent health. He had smoked one package of cigarettes per day for the past forty years.

Physical examination revealed a thin, markedly pale man, who appeared wasted and weak but not in distress. There were limited excursions of the chest, dullness, decreased breath sounds and fremitus below the seventh to eighth rib on the left and a few moist rales at the right base. Examination of the heart was unremarkable. There was a firm subcutaneous nontender movable 3-cm. mass under the right nipple that was not fixed to ribs or skin. The liver was palpated 1 fingerbreadth below the right costal margin and was nontender. No tenderness or definite masses were noted in the abdomen, although a vague ill-defined sense of resistance was noted in the right upper quadrant. There was definite clubbing of the fingers and toes.

The temperature was 99.5°F., the pulse 100 and the respirations 40. The blood pressure was 135 systolic and 80 diastolic in both arms.

Examination of the blood showed a hemoglobin of 8.5 gm., a red-cell count of 3,350,000, with normochromia and a moderate degree of anisocytosis, and a white-cell count of 14,100, with 70 per cent neutrophils. A stool guaiac test was +++ on admission and one week later was reported as +. The serum nonprotein nitrogen was 16 mg., the alkaline phosphatase 2.5 units and the total protein 7.4 gm. per 100 cc. The prothrombin time was 21 seconds (normal, 17 seconds) (68 per cent). The blood Hinton test was negative. A cytologic study of the sputum was negative for malignant cells. An electrocardiogram was within normal limits.

X-ray films of the chest showed a fair-sized pleural effusion on the left. The left lower lobe was considerably reduced in size. Air could be followed in the left-lobe bronchus to a point approximately 5 cm. beyond its origin, at which level it appeared to end rather abruptly. The medial wall of the bronchus appeared irregular. The rest of the left lung and the entire right lung appeared clear. The lower third of the thoracic esophagus deviated sharply to the right (Fig. 1). No bone destruction was seen. The heart did not appear enlarged. A gastrointestinal series, barium-enema examination and sigmoidoscopy were within normal limits.

On the third hospital day a thoracentesis of the left chest yielded 200 cc. of thick, light chocolate-colored material that had a sweetish odor and a specific gravity of 1.050. A smear showed occasional gram-positive cocci in chains. No acid-fast bacilli were seen. *Staphylococcus albus* and anaerobic streptococci were cultured. Three days later another chest tap returned 25 cc. of thick, turbid, pale pink, foul-smelling fluid, which grew anaerobic streptococci on culture. Three hundred thousand

units of penicillin were instilled in the chest cavity at this time, with 10 cc. of methylene blue. The dye appeared fifteen minutes later in the sputum. Bronchoscopy showed the carina to be reddened and partially fixed but not deviated. The lower-lobe bronchus near the terminals bled easily and was somewhat granular and partly fixed. A biopsy showed normal cartilage. Cytologic examination of bronchial washings was unsatisfactory.

After the instillation of penicillin in the pleural cavity 300,000 units of Crysticillin was administered intramuscularly twice daily. The temperature, which had ranged from 99.5 to 101°F., gradually returned to normal within five days. Three whole-blood transfusions were given, and the hemoglobin rose to 11 gm.

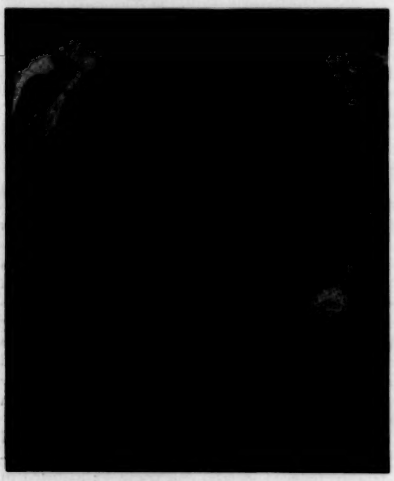

FIGURE 1.

An operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. F. DENNETTE ADAMS*: The problem boils down to three alternatives: Am I dealing with infection alone — and if so, what kind of infection? Is it infection behind bronchial obstruction, presumably due to tumor? If tumor, is the disease primary in the thorax or metastatic?

What history of onset is given me is not sufficient to justify a diagnosis of pneumococcic or any other form of bacterial pneumonia. One would be highly suspicious of this if given a history of sudden onset with high fever, bloody or rusty sputum, chill or pleural pain. The vague character of onset introduces the possibility of virus pneumonia. The physician who first saw the patient might have been justified in thinking in terms of virus or atypical pneumonia, with secondary pleural fluid. However, the subsequent course makes this diagnosis unlikely. Although pleural effusion is not uncommon in virus pneumonia, suppuration, in my experience, is rare. The patient became anorexic and extremely weak — so weak, in fact, that even when he felt a little better he did not get out of bed. He lost 12 pounds in a relatively short time. These symptoms could have been due to infection alone, but they seem to have been somewhat more severe than one would expect in this period from bronchopulmonary pleural infection alone. The blood-tinged sputum could have resulted from chronic infection but could just as likely have resulted from a malignant process in a bronchus. The story of grippe late in the disease seems open to some question. One wonders if the increase of symptoms at the time was not due to increased bronchial obstruction, with greater backing-up of infection. The right-lower-quadrant pain occurring after meals is not well defined. It is hard to decide how much attention one should give it. To summarize the history: This man with obvious bronchopulmonary pleural infection went downhill fairly rapidly and later developed some pain in the right lower quadrant.

In the physical examination there was no mention of edema of the ankles. Had it disappeared by the time of admission?

DR. HELEN S. PITTMAN: He had no edema of the ankles after he came into the hospital.

DR. ADAMS: The physical examination was not very helpful. This man showed signs of loss of weight and weakness; the respirations were increased, he was running fever and he had signs at the left base that one could attribute either to fluid or to thickened pleura. If the breath sounds were only diminished, one would favor thickened pleura; if they were absent, fluid would be more likely. We know from the chest taps that fluid was present. The nodule is important. One must keep in mind that he cannot be sure that it was not a wen that had been present for years but was discovered by the patient only when he became thinner. The prostate, I assume, was examined and found to be negative.

DR. PITTMAN: Yes.

DR. ADAMS: The laboratory tests give me no definite clues. The blood chemical levels were all right. The normochromic anemia would be disturbing if the man had not been receiving iron; this medication may well have kept him from developing hypochromia along with the drop in the red-cell count, which would be expected with chronic infection or malignant disease. In fact, the one grossly abnormal laboratory finding serves only to confuse the issue. Why should a man with

*Physician, Massachusetts General Hospital.

bronchopulmonary disease have a +++ guaiac test on the stool? It is hard to believe that this could be due to the amount of blood-tinged sputum that he might have swallowed. If the observation was correct, one is almost forced to conclude that he had a bleeding lesion somewhere in the gastrointestinal tract.

How much can the radiologist help me? Attention must be called to the fact that here was a man with a proved fistula who had no signs, by physical or x-ray examination, of air in the thoracic cavity along with the fluid. This paradox is likely explainable by the fact that the films were taken and the physical examination performed before the fistula developed. Whether there was a spontaneous rupture or the leak was created by the first tap no one can say.

DR. WILLIAM R. EYLER: These films show the pleural effusion in the left chest and the density in the region of the left lower lobe. The problem here was to decide the nature of the lesion that you see at the end of the air column in the left-lower-lobe bronchus. The column of air terminates fairly abruptly approximately at the point of division of the bronchus, and there is a suggestion of some irregularity in the bronchial wall just above the point at which the air column terminates. I see no evidence of definitely enlarged intrathoracic lymph nodes.

DR. ADAMS: The protocol reports, — and if one looks closely one can see, — that the esophagus is pushed to the right.

DR. EYLER: It is definite but probably not significant, in view of the presence of the fluid.

DR. ADAMS: Do you think that amount of fluid would push the esophagus so far?

DR. EYLER: I think it could.

DR. ADAMS: I shall accept your word for it. I would have thought more fluid would be needed to push the esophagus over.

DR. EYLER: I cannot exclude a lesion in that region.

DR. ADAMS: Neither can I.

Now let us return to the questions posed at the start: Was it infection alone; was it bronchial obstruction with secondary infection behind it; and if the latter, was the tumor primary or metastatic? A few less likely diagnoses should be mentioned in passing. Actinomycosis could perhaps cause this picture, but there certainly was no evidence for it. So could a foreign body, but again we have no evidence. Once, at one of these conferences, I made a diagnosis of carcinoma of the lung in a case of lipoid pneumonia, so that disorder, too, should be named as one of the more remote possibilities. As the record states, this patient had always been in excellent health, so it is unlikely that he was in the habit of putting oil drops in his nose. As his bowel movements were regular he probably did not take mineral oil.

I doubt if one could explain this illness entirely on the basis of infection. We have no clear-cut history of pneumonia; the man was, as already stated, somewhat more weak and incapacitated than one would expect with infection alone. Since he developed a nodule in the chest wall, a diagnosis of bronchial obstruction due to malignant tumor seems more tenable. Whether the tumor was primary or metastatic is anybody's guess. There is little to point to an intra-abdominal lesion, but one cannot disregard the right-lower-quadrant pain and the +++ guaiac stool test. These suggest a lesion within the abdomen. The ill-defined right-upper-quadrant resistance mentioned in the physical examination is not sufficiently clear-cut to be of help. Carcinoma of the cecum with metastasis to the lung is a distinct possibility. We know that malignant disease of the cecum will remain silent for a long time, that it does bleed and that it often metastasizes to the lungs and elsewhere.

It is entirely a toss-up whether one puts the primary lesion in the lung or in the abdomen, — and if one does the latter, whether he puts it in the cecum or in the pancreas. The ground rules require a diagnosis; so, mostly because of the positive guaiac test and the right-sided pain, I will make a diagnosis of metastatic malignant disease of the lung, probably primary in the cecum. I would just as readily settle for one in the pancreas or for a primary carcinoma in the lung. One more factor that leads me toward malignant disease rather than infection alone is the displacement of the esophagus, which, in my opinion, is due more likely to tumor or to enlarged mediastinal lymph nodes from tumor than to fluid.

DR. EDWARD B. BENEDICT: Widening and fixation of the carina usually means cancer that invades the lymph nodes in the mediastinum. The carina was definitely widened and partially fixed. There was some fixation of the left lower bronchus, too, which is also indicative of cancer. I favored a primary carcinoma of the bronchus.

DR. JACOB LERMAN: Would you assume that the lump in the breast was a malignant nodule?

DR. ADAMS: That is open to question. As I said, maybe the patient had a wen that he never felt until he lost all this weight.

DR. LERMAN: It could be gynecomastia.

DR. ADAMS: It was not in the nipple; it was below the breast.

A PHYSICIAN: It was right under the nipple.

DR. ADAMS: Deep inside the nipple?

DR. PITTMAN: I described it as a small breast mass, loosely adherent beneath the areola.

A STUDENT: Would the guaiac test be +++after oral administration of iron?

DR. ADAMS: He had had iron just before he came in, but the record does not state for how long. I wish someone would tell me once and for all how often positive guaiac tests are obtained after iron

therapy. I have been sweating over that one for a long time and have never been sure.

Dr. Marian W. Ropes: I have no idea how high the percentage is, but I do know that positive tests have been obtained after iron. They can be differentiated by removing the ether layer before completing the test. The iron does not go into the ether layer, and there is not a positive reaction if the ether layer does not remain on the stool. I have no idea how often it happens, and I would expect it would never be +++ to ++++; it is usually + or ++.

Dr. Lerman: The reason I raised the question of gynecomastia is that we have seen primary carcinoma of the bronchus with gynecomastia.

Dr. Adams: That is something I did not know. Bilateral or unilateral?

Dr. Lerman: Gynecomastia sometimes can be unilateral, but usually the other breast is involved.

Dr. Pittman: We were not much concerned about the breast. That seemed unimportant and irrelevant, at least to the other trouble. It was one of those nasty findings that one turns up when one does a thorough physical examination. We were worried about the chest, wondering whether it was pure infection or infection beyond tumor. We were particularly worried when we obtained the chocolate-colored fluid from the pleural cavity. When he had such a definite evidence of bronchopleural fistula after the methylene blue was instilled we decided that it probably was not tumor but that the hemoglobin in the fluid had come from the process that caused the fistula. We thought the weight loss might have been explained by the infection of the chest and by the anemia of 8.5 gm. A complete gastrointestinal series and a sigmoidoscopy were carried out. They were all entirely normal. On one film the cecum was full of fecal material. The stool gradually ceased to show a positive reaction.

Clinical Diagnosis

Empyema with bronchopleural fistula secondary to inflammatory lesion in lung or bronchus.

Dr. Adams' Diagnosis

Metastatic carcinoma of lung from cecum, ? from pancreas.

? Primary carcinoma of lung.

Anatomical Diagnosis

Empyema with bronchopleural fistula.

Pathological Discussion

Dr. Edward D. Churchill: From the diagnostic standpoint we explored most of the arguments that Dr. Adams has laid before you, although the simple entity of an encapsulated empyema following an upper-respiratory infection was highest on the list. In Medical Grand Rounds this morning the whole question of present-day management of localized empyema was under discussion. We see empyema so rarely today that when we do our thoughts turn not to the old picture of postpneumonic empyema but to some disorder that prevents the patient under antibiotic therapy from throwing off the infection and absorbing the exudate. The situation is not too different from left-sided paracolic abscess — the spontaneous collection of pus in the belly — which is not recognized as an entity but which immediately brings to mind diverticulosis with infection, carcinoma with surrounding inflammatory disease, or a localized regional enteritis. It is the same with the chest. It is essential to consider what is going on in the underlying lung that causes the empyema to encapsulate instead of fading away.

There are two or three different methods of management to be evaluated. There is the simple and direct method of taking out a small segment of rib, finding the pus and putting in a drainage tube. Ultimately the tube may be removed when the cavity has been obliterated. There is also the temptation to treat a localized empyema by what is called the "medical" method; that is, repeated aspiration. If one believes that there is a large mass of fibrin, its dissolution may be effected by the use of streptokinase and streptodornase and then an attempt may be made to "sterilize" the cavity by the local introduction of antibiotic agents. In this case we followed neither of these proposals but performed thoracotomy so we could actually visualize the lesion. An empyema cavity was exposed that contained malodorous pus, which indicates a mixture of many organisms from which culture may identify only one or two species. Undoubtedly a good many different organisms were present. It was possible to excise the thick capsule of the encapsulated area of pus. After this was removed the lower lobe could be examined carefully. It looked somewhat battered; that is, it showed some leaks, presumably where the methylene blue had seeped into the bronchi, but there was no bronchial fistula. The lower lobe was carefully palpated to check from the outside what Dr. Benedict had observed from the inside at bronchoscopy. The hilar lymph nodes appeared soft and inflammatory. We found no evidence of tumor or of bronchiectasis. The lobe inflated well when the pressure was increased within the endotracheal anesthesia system. The empyema had caused a tremendous distortion; it had twisted the lobe upward and made it adherent in an abnormal position. The goal was to straighten out the lobe and give it the optimal chance to resume functional activity.

What we are attempting is an appraisal of the relative merits of the methods of management of encapsulated empyema with the aid of antibiotics and present-day technics. In some we may elect to use the repeated aspiration method; in others,

simple drainage; and in still others, the more radical excision illustrated in this case.

DR. BENJAMIN CASTLEMAN: As Dr. Churchill has just stated, we found no evidence of carcinoma anywhere. We examined the specimen carefully for any specific organisms. There was no evidence of any granulomatous reaction, such as one might find with tuberculosis or perhaps with a foreign body. We looked for actinomyces and were unable to find any. We were then left with the diagnosis of a nonspecific type of infection. There was much evidence of old inflammatory reaction with a great deal of necrosis and fibrosis as well as the acute infection. The blood vessels were very thick, showing that infection had been there for a long time.

DR. CHURCHILL: This patient was discharged with primary healing of the incision and, as far as we know, ablation of the disease on the thirteenth postoperative day.

DR. CASTLEMAN: Before he left the hospital the surgeons removed the lump in the breast and sent it to the laboratory. It was gynecomastia.

CASE 37262

PRESENTATION OF CASE

A forty-seven-year-old man entered the hospital because of abdominal pain, nausea, vomiting and shock.

Twenty-four hours before admission, at about 7:00 p.m., the patient was seized with epigastric pain "like a great ball" that quickly radiated upward through the chest to the back of the neck and top of the head, down the left arm to the elbow and downward through the chest, "first to the left kidney and then to the right." The patient stated that he had had "pain in the kidneys" before. He was seen by his physician, who said that he had "epigastric pain radiating to the left arm without nausea or vomiting" and administered morphine. The blood pressure was 146 systolic, 90 diastolic and the pulse 86. The abdomen was said to be flaccid without tenderness. The patient spent most of the night awake because of continuous severe periumbilical pain that was not relieved by frequent vomiting. On the next morning he noticed bright-red blood in the stool. Another similar stool was later verified by his physician. The physician examined him again and referred him to this hospital because the patient had no pulse or blood pressure and was thirsty, sweating and cold. The patient walked into the Emergency Ward and was immediately put to bed.

At the age of eighteen the patient had an attack of rheumatic fever (manifestations unknown). One year before admission, according to the patient's physician, he had congestive failure with dyspnea and edema. He was digitalized and apparently responded so that he was able to work until the time of the present episode. The patient stated that his blood pressure in the past had been as high as 180 systolic, diastolic unknown. He had been a heavy drinker. The last bout of drinking was five days before admission. He frequently had heartburn, with pain that waked him at night and was relieved by taking soda.

Physical examination revealed a short, heavy-set, cyanotic, sweaty man with clammy skin. The heart revealed gallop rhythm and distant and regular sounds; no murmurs were heard. The lungs were free of rales anteriorly. The abdomen showed epigastric fullness with some tenderness on deep palpation, absent peristalsis and hyperactive abdominal reflexes. The rectal examination revealed slight anterior tenderness, especially on the left side, and a slightly tender prostate.

The temperature was 100°F. orally, the pulse 120 and the respirations 30. The blood pressure was unobtainable.

The urine had a specific gravity of 1.020 and gave a + test for albumin and a + test for sugar; the sediment contained an occasional white cell and epithelial cell. Examination of the blood showed a hemoglobin of 17 gm. and a white-cell count of 7350. The stool was red and gave a ++++ guaiac reaction.

X-ray films of the chest showed an area of relatively homogeneous density in the lateral segment of the right middle lobe. There was a small amount of fluid in each pleural space. The left heart border was not sharply defined, but this may have been the result of atelectasis in the lingula of the left upper lobe. The pulmonary vessels were not unduly prominent. The heart was very large, with predominance of the left ventricle. The aorta was poorly seen but appeared to be somewhat elongated. The superior mediastinum was rather wide, and there was indentation of the trachea in the suprasternal notch. The aortic arch could not be well followed (Fig. 1). Abdominal outlines and bone densities were not unusual. There was a small amount of air in the large bowel and some dilated loops of small bowel in the left abdomen.

One observer noted that the patient had cyanosis, predominantly over the upper half of the body, with slow return of color after pressure. An abdominal tap made shortly after admission revealed 1 cc. of turbid yellow fluid. Later that night the white-cell count rose to 15,000. The sodium was 146 milliequiv., the chloride 101 milliequiv., the calcium 4.9 milliequiv. and the carbon dioxide 21.4 milliequiv. per liter; the fasting blood sugar was 54 mg., the nonprotein nitrogen 60 mg. and the serum amylase 16 units per 100 cc. A repeat test showed the serum amylase to be 29 units per 100 cc. Two electrocardiograms, made on entry and four hours after entry, revealed a sinus tachycardia at a rate of 110, a PR interval of 0.12 second and a QRS interval of 0.06 second. The T waves were

depressed in Leads 1, 2, AVL, AVF, V_4 and V_6 and diphasic in Leads V_1, V_2 and V_3. The ST segment was depressed in Leads V_4 and V_5. Another examiner noted that there were no palpable carotid, axillary, brachial, radial, popliteal, dorsalis-pedis or posterior-tibial pulsations but a right temporal pulse could be felt and femoral pulses were fair. The neck veins were noted to be flat. The lungs were clear except for a few moist rales at the bases posteriorly. Neurologic examination was negative except for slightly hypoactive reflexes.

On the following day another examiner noted an occasional faint variable brachial-artery pulse

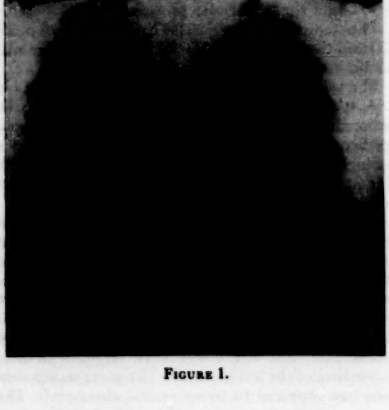

FIGURE 1.

on the right, good bilateral femoral pulsations and no carotid pulsations. Still later, on the second hospital day, strong bilateral femoral pulses, a faint dorsalis-pedis pulse on the right and a faint variable right-brachial pulse were felt. No definite pulsations of the right and left carotid artery were noted. There was marked cyanosis of the neck, upper chest and face and marked cyanosis over the lower trunk and extremities. A harsh Grade II systolic murmur was heard in the aortic area for the first time. The abdomen was noted to be soft and diffusely tender, with greater tenderness just below the umbilicus. A few faint peristaltic tinkles were heard. Later on the same day another examiner noted a faint aortic diastolic murmur. A urine specimen was insufficient for determinations of specific gravity, albumin and sugar. The sediment was loaded with epithelial cells and contained frequent white cells and occasional red cells. On the third day the patient was anuric. The blood pressures, obtainable on the left arm only, were 110 to 120 systolic and 70 to 80 diastolic and later that day dropped as low as 80 systolic, 60 diastolic. A diagnostic pericardial tap was made below the left paraxiphoid region. Ten cc. of fluid, which appeared to be pure blood that was not under pressure and did not clot, was removed. The patient lapsed into coma, with the temperature gradually rising to 105°F. and the respirations to 50, and died on the third hospital day.

DIFFERENTIAL DIAGNOSIS

DR. VICTOR G. BALBONI*: Before discussing this case, may I see the x-ray films, Dr. Wyman?

DR. STANLEY M. WYMAN: The films were taken in the upright position with the tube as near to 6 feet from the patient as possible, so there is very little magnification of the heart shadow. The heart is tremendously enlarged, particularly in the region of the left ventricle. The aortic contour is poorly seen and the aortic arch appears rather hazy in outline. There is a suggestion of some calcification in the aortic arch, but this is not certain. There is a rather sharp angular bulge in the expected location of the proximal ascending aorta. This is present on two films. There is also some soft-tissue fullness in the superior mediastinum, compressing the trachea, as noted in the record. The hazy density described in the middle lobe is well seen and lies against the fissure between the middle and lower lobes (Fig. 1). The plain film of the abdomen shows several loops of gas-filled, somewhat distended small bowel, but one can draw no definite conclusions from it. The patient was very sick.

DR. BALBONI: Would you say that the wall of the bowel was edematous or thickened, suggesting the "lead-pipe" appearance of infarcted bowel?

DR. WYMAN: It does not look too remarkable, but it is somewhat risky to attempt a definitive opinion on this type of film.

DR. BALBONI: When a patient has as widespread symptoms and findings in so many systems of the body as this one had, it seems to me that the differential diagnosis can be boiled down to either metastatic malignant disease affecting various areas of the body or some form of diffuse vascular disease. There is nothing in the past history and symptoms that suggests that this man had cancer, so I think we can discard that as a possibility and turn to some form of vascular disease. The history and physical findings are pathognomonic of only one type of vascular disease, namely, dissecting aneurysm of the aorta. The factors in this case leading me to reach this diagnosis I shall take up one by one.

This man was in the proper age group — he was forty-seven. The mean average age at which dissecting aneurysm of the aorta occurs is about fifty-five, but it not uncommonly occurs in the late forties. Dissecting aneurysm of the aorta is much more common in men than in women — about three times as common, I believe. This man had known

*Assistant in medicine, Massachusetts General Hospital.

hypertensive vascular disease in the past, and almost all patients who develop a dissecting aneurysm of the aorta have had hypertension preceding the dissection. The history suggested that this man may have had rheumatic fever, but no murmurs were heard at first, so I can assume that he did not have rheumatic heart disease.

The most characteristic feature in the history that suggested dissecting aneurysm of the aorta was the onset of symptoms. Pain is usually a very prominent symptom in dissecting aneurysm. The pain is never quite the same in any two cases; it does not always follow exactly the same pattern but comes on suddenly, is very severe and may radiate to the back, occasionally to the head and frequently to the abdomen. This man had all these types of radiation. The pain does not always begin in the chest but may begin in the abdomen. Then this patient developed evidence of some disturbance in the bowel, which suggests mesenteric thrombosis to me. He had bloody stools and developed ileus; that is not uncommon in dissecting aneurysm of the aorta because, although the dissection usually begins in the ascending aorta 1 to 2 cm. above the aortic valve, the process almost invariably extends down the descending aorta, involving various branches. Presumably, in this case, the superior or inferior mesenteric artery was affected, causing a thrombosis of that vessel — either partial or complete. No pulses were felt in the upper extremities, and on the day of entry his physician could not obtain the blood pressure. The patient was said to have been in shock. However, he walked into the Emergency Ward, so the shock could not have been very severe. I think the dissection had partially occluded the innominate and the subclavian arteries at the arch of the aorta and that is why the blood pressure was not obtainable in the arm at that time.

In the hospital the patient ran a low-grade fever and had a leukocytosis, — two things that customarily occur in dissecting aneurysm of the aorta. The blood chemical determinations were normal except for the sugar, which was low — probably because the patient had not eaten anything. Later in the course of the illness red cells appeared in the urine and the patient became anuric, which indicates that the dissection had proceeded down the aorta and involved the renal arteries. All in all, the clinical picture seems to be well explained by this condition.

The finding in the lung suggests an infarct; I cannot quite explain that, although in some cases of dissecting aneurysm of the aorta blood has dissected down outside the pulmonary arteries into the lung fields; that may have been what occurred here.

In a differential diagnosis of a dissecting aneurysm of the aorta, the question of myocardial infarction always arises. In this case the onset of the pain was not characteristic of a myocardial infarction; it was too severe, and its radiation was unusual for infarction of the heart muscle. The electrocardiographic tracing I interpret as left-ventricular strain. Since if this was an infarct it must have been a massive one, I would expect more classical electrocardiographic changes of infarction than were found here. If he had an infarction of the heart one would have to assume that mural thrombi had formed and were thrown off as emboli that occluded the various vessels that had been affected. Ordinarily, in myocardial infarction, mural thrombi with emboli do not develop so rapidly as this, certainly not for three or four days. In this case on the morning after the onset of pain the patient already had no pulses in the upper extremity, so I think one can discard that possibility. Since he had had rheumatic fever one might consider the possibility that he had been fibrillating and had thrown off multiple emboli from a fibrillating heart. However, there was nothing in the record to indicate that he was fibrillating, so I do not think that we can seriously entertain that possibility, either.

Terminally a pericardial tap was done and blood was found in the pericardial sac. There is good evidence that the tap was made into the pericardial sac and not into the heart, as we learn from the record that the fluid was not under pressure and did not clot. In dissecting aneurysm of the aorta, — although the original dissection goes up the arch, down the descending aorta and into the iliac vessels, — the dissection frequently may also extend backward to the aortic rim and then rupture into the pericardium, causing death. Often, when the dissection spreads backward, the coronary arteries may be occluded and myocardial infarction may occur secondarily; that possibly happened here.

Dissecting aneurysm of the aorta is a disease of unknown etiology. It apparently is not related to syphilis, to previous rheumatic heart disease or to a generalized arteriosclerosis but seems to be due to a cystic degeneration in the media. This man had some other symptoms. He had been a heavy drinker, but there was nothing on which to base a diagnosis of cirrhosis of the liver, and there was certainly nothing in the history to suggest that. He had some heartburn, which was relieved by soda, but no other symptoms that would lead to a diagnosis of ulcer of the stomach. If he had an ulcer, it would have been a secondary condition. Having put myself out on a limb and sawed the branch off, I should like to close with the diagnosis of dissecting aneurysm of the aorta.

Clinical Diagnosis

Dissecting aneurysm of aorta.

Dr. Balboni's Diagnosis

Dissecting aneurysm of aorta.

Anatomical Diagnoses

Dissecting aneurysm of aorta and the innominate, left subclavian, left carotid and both common iliac arteries.

Fatty degeneration of the myocardium due to anoxemia.

Central necrosis (partial infarction) of the liver.

Acute parenchymatous degeneration of right kidney (anoxemic).

Subpleural and interstitial hemorrhage of lungs.

Pathological Discussion

Dr. Tracy B. Mallory: This man did have a dissecting aneurysm, as predicted. Dr. Alexander S. MacMillan has drawn a diagram of his findings on the board (Fig. 2). The heart, as one would expect, was markedly hypertrophied; it weighed 700 gm. It showed a bicuspid aortic valve with very marked calcification, and some degree of stenosis. As Abbott* pointed out many years ago, there is a more frequent association between bicuspid aortic valves and dissecting aneurysm of the aorta than would be expected on the laws of chance, so probably there is an etiologic relation. The mitral valve did not show any clear rheumatic involvement. There was no shortening or thickening of the chordae, although there was evidence of slight old chronic inflammation on microscopical examination that was consistent with but not diagnostic of rheumatic involvement. There were also some old fibrous pericardial adhesions, which might likewise have been of rheumatic origin. Evidently, if there was rheumatic disease it was purely coincidental.

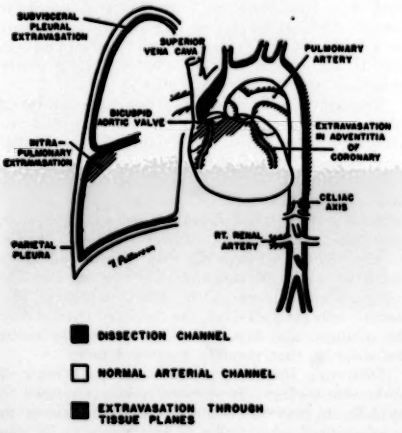

Figure 2.

The dissecting aneurysm was based, as usual, on disease of the aortic media, so-called medionecrosis cystica. There was a V-shaped tear of the intima on the posterior aspect of the ascending aorta, and the dissection had spread up over the arch and down the descending aorta as far as the iliac vessels—even extending a short way along each iliac vessel. In this diagram the solid black represents the plane of dissection, which at autopsy was found filled with clotted blood. The unshaded portion is the original aortic lumen. The dissection had spread a short way along the innominate, internal carotid and subclavian arteries, but rerupture into the lumen of the vessel had not occurred in these arteries. This would adequately explain the total physiologic occlusion of these vessels during the terminal period of life and the complete absence of pulse or detectable blood pressure. When rerupture back into the original vascular lumen occurs in the iliac arteries the high pressure in the external cleavage plane will drop and the intima of the vessel will no longer be pushed sharply inward to produce occlusion, so the pulse may then return in the vessels of the upper extremities, as was reported. In these cases of dissecting aneurysm it is frequently evident that one or more of the aortic branches have been occluded for some time. In some cases, as here in the case of the innominate, subclavian and carotid arteries, this is due to extension of the dissection along the branches. In general this occurs only in vessels that have an elastic structure similar to that of the aorta itself. Muscular arteries, such as the coronary and renal arteries, do not ordinarily suffer dissection. However, they too may be occluded, as a segment of the vessel must pass through the new blood channel, where it is subjected to external pressure greater than that of the lumen of the small artery. It is impossible, by looking at the anatomic specimen at post-mortem examination, to say whether or not the vessels were in fact occluded, unless secondary thrombosis has developed. One can only infer it from the evidence of degenerative changes in the tissues and organs supplied by the given vessel. Evidence of this sort was found in this case in several organs. The myocardium was slightly abnormal in appearance. The man who examined the organs grossly was in doubt, and when the specimens were reviewed in conference there was some difference of opinion concerning whether or not there was necrosis of the myocardium, but a fat stain showed extensive fat vacuolization of the muscle cell — a type of change that occurs very quickly as the result of anoxemia.

Another interesting and relatively unusual change was in the liver. This showed decided exaggeration of the markings. The picture resembled the so-called "nutmeg liver" of chronic passive congestion, but we have no confirmatory evidence of long-stand-

*Abbott, M. E. Congenital cardiac disease. In *Osler's Modern Medicine.* Vol. 4. 1011 pp. Philadelphia: Lea and Febiger, 1927. P. 747.

ing passive congestion in this case. Microscopical examination showed that there was in fact extensive necrosis of the central third of every lobule — again a type of change that is characteristic of severe anoxemia. It could in fact be considered infarction, because the liver, with its double blood supply, never undergoes complete infarction, as do the heart and the kidneys, which have terminal arteries. Some cells are always kept alive by the portal circulation, but the cells at the center of the lobule nevertheless are destroyed when the arterial blood supply is shut off. As far as I can remember from the history, there was nothing to suggest liver failure, although it seems that some must have been present. The kidneys likewise were abnormal in appearance and quite different from each other. The left was extremely pale and showed areas very suggestive of infarction. The right, in contrast, was decidedly congested and looked somewhat hemorrhagic. There had been almost complete anuria in the terminal stages of the illness.

One other rather striking anatomic feature of the case, which is common in similar cases, was extensive hemorrhagic extravasation in the interstitial tissue of the lung, particularly in and just beneath the pleura as well as around the blood vessels and in the peribronchial tissues (shaded area, Fig. 1). In some places, these areas looked at first glance almost like pulmonary infarctions, but on closer examination it is evident that there was actually no lung tissue within the area but simply a focal collection of blood in the loose fibrous tissue of the lung stroma. I think these changes adequately account for some of the shadows seen in the x-ray film — particularly the ones in the region of the interlobar septa, where many of the hemorrhages were concentrated. I doubt that they had functional significance as far as ventilation or gaseous exchange was concerned. There were no gross abnormalities in the brain. Unfortunately the spinal cord was not removed. I think it is quite likely that there was anoxemic damage there. Would that fit with the absent reflexes and paralysis, Dr. Kubik?

Dr. Charles S. Kubik: I think it is quite possible, although in the one case that I recall the paralysis was due to the obstruction to the flow of blood through the iliac artery.

Dr. Jacob Lerman: Was the necrosis of the ileum the result of mesenteric thrombosis or mesenteric occlusion?

Dr. Mallory: No thrombosis was found. There was hemorrhagic necrosis of the lower small bowel, the cecum and part of the ascending colon, which I think makes it quite certain that there was functional closure of the inferior mesenteric artery for a significant period of time.

Dr. Balboni: How do you think the blood got into the lung? Did it dissect down along the pulmonary artery, and if so how did it get next to the pulmonary artery?

Dr. Mallory: It worked its way out into the loose mediastinal tissues, which are more or less continuous with the perivascular and peribronchial tissues in the lung. There was evidently a very easy plane of cleavage.

Dr. Balboni: If the aorta was not actually ruptured, where did the blood found in the lung come from?

Dr. Mallory: In any case of rupture there is likely to be rather extensive extravasation of blood into neighboring tissues. You may or may not be able to find an obvious point of perforation in the adventitia of the aorta. Very extensive extravasation can occur without any tear that can be demonstrated by probing. I forgot to mention that one area where extravasation was particularly severe and extensive in this case was the anterior mediastinal fat pad — the region that is occupied in infancy and childhood by the thymus and replaced in adult life by ordinary adipose tissue but always maintains the general shield-shaped outline of the thymus gland. This, I believe, would account for at least part of the widened mediastinal shadow. A widening of the aortic arch, due in part to thickening of the walls of the aorta, would unquestionably be another factor. There was also, in this case, a rather diffuse ectasia of the ascending aorta, a not uncommon finding in patients with hypertension, having no direct bearing on the question of the dissecting aneurysm.

The New England Journal of Medicine

Formerly

The Boston Medical and Surgical Journal

Established 1828

Official Organ of
The Massachusetts Medical Society
and
The New Hampshire Medical Society
Owned by the Massachusetts Medical Society and Published Weekly under the Jurisdiction of the Committee on Publications

Richard M. Smith, M.D., *Chairman*
James P. O'Hare, M.D. Conrad Wesselhoeft, M.D.
Oliver Cope, M.D. John Fallon, M.D.

Joseph Garland, M.D. Editor

Associate Editors
Thomas H. Lanman, M.D. Donald Munro, M.D.
Theodore H. Ingalls, M.D.

Clara D. Davies, Executive Editor
Robert O'Leary, Assistant Editor*

Editorial Board
C. Guy Lane, M.D. Maxwell Finland, M.D.
Henry R. Viets, M.D. C. Stuart Welch, M.D.
Robert M. Green, M.D. Vernon P. Williams, M.D.
Dwight O'Hara, M.D. Benjamin Castleman, M.D.
Fletcher H. Colby, M.D. Hugh R. Leavell, M.D.
Robert L. Goodale, M.D. J. Englebert Dunphy, M.D.
Chester M. Jones, M.D. Robert W. Buck, M.D.
Harvey R. Morrison, M.D. Herman L. Blumgart, M.D.
Deering G. Smith, M.D.†

*On leave of absence with the Armed Forces.
†Representing the New Hampshire Medical Society.

Subscription Terms: $8.00 per year in advance, postage paid, for the United States (medical students, $4.00 per year); Canada, $9.00 per year (Boston funds); foreign, $10.50 per year.

Microfilm volumes available to regular subscribers through University Microfilms, 313 N. First Street, Ann Arbor, Michigan.

Material, other than original articles, should be received not later than noon on Thursday, three weeks before date of publication.

The Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston 15, Massachusetts. Telephone KE 6-2094.

HOSPITAL AND PROFESSIONAL RELATIONS

There is no question that the lay trustees of a privately endowed hospital have the legal power to name the physicians who may use the facilities of the institution and to deny its use to any physician at their discretion.

Use of this power, however, may lead to conflict and recrimination, — and indeed has done so in a number of instances. Physicians of Massachusetts are generally familiar with the case of the sectarian hospital that did not choose to permit advocates of planned parenthood to remain on its staff, and there is the more recent instance of a hospital that has refused to retain several physicians for reasons not publicly stated, which has engaged the attention of the Council of the Massachusetts Medical Society.

In the present allegedly poor state of medical public relations it is important that physicians keep their heads and carefully consider their course of procedure in such misunderstandings. They must obey their consciences, and they must also think of the effect on a possibly incompletely informed public of whatever action they take.

Anything like a "strike," such as might be called by laboring men who believe that they are unfairly treated by their employers, is not to be considered. The first duty of the physician is to his own patients and to those other patients of the hospital that may be under his care.

A few purely hypothetical possibilities may be reviewed.

Let it be supposed that a staff physician has said or done certain things that are repugnant to the tastes, prejudices or morals of the trustees and the trustees request his resignation. In such a case, the physician may issue a statement in defense of his speech or conduct; the trustees, if they choose, may do the same, and the public may judge which has the better case. Public opinion may or may not induce the trustees to rescind their vote.

Suppose, on the other hand, that the policies of a hospital, as dictated by the trustees, are repugnant to the moral, ethical or professional standards of a staff physician. His only choice, if the trustees cannot be converted to his point of view, is to resign from the hospital staff. Here again there is no objection to full publicity and an appeal to public opinion.

A third unpleasant possibility is that the physicians of the staff are themselves divided, some supporting a fellow member who is in difficulties with the board of trustees and others supporting or even instigating the action of the trustees, possibly with selfish motives. To air this sort of quarrel publicly may be unwise. There may be well known but unprovable facts and accusations that would better be discussed privately. A possible solution might be found in mediation by a third party. However, in this event it is quite possible that wrong might at least temporarily prevail and innocent victims be forced to suffer in silence.

In any of these possible situations, there can be no objection to the staff physicians' individually following the dictates of their own consciences. If the issue is clear-cut and the physicians agree that the trustees are at fault, they may or indeed should resign. The action need not be precipitous, and no patients need be neglected. There is no question of a "strike." If all the physicians of a hospital resign and the trustees seek to replace them with others who are more amenable to their demands, effective action is still possible if the issue is clear and unmistakable. Physicians who are willing to compromise their standards for the sake of a position on such a hospital staff might well be disciplined by the medical society.

It is not otherwise reasonable to expect medical societies to adjudicate issues that are primarily between the staff of a hospital and its trustees, except as the societies are a part of the public to which either side may appeal.

TUBERCULOSIS CONTROL PROGRAM

MEDICAL installations developed for the purpose of controlling disease must be prepared from time to time to take stock of themselves, to evaluate their efforts and at times even to consider whether they have any justification for further existence. The effectiveness of any such institution, whether it be public or private, is best measured not by the opinion of the personnel who run it — for they are naturally, almost necessarily, prejudiced observers — but by consultants with access to objective epidemiologic data by which accomplishment can be quantitated. With such general considerations in mind, a study of Boston's health needs and services made by Dr. Russell F. Teague, consultant in tuberculosis to the United States Public Health Service, in 1949, was reviewed in March, 1951, by a committee appointed by the Division of Health, Hospitals and Medical Care of the United Community Services to study the Boston Tuberculosis Control Program. With Dr. Theodore L. Badger as its chairman and Dr. Alton S. Pope, deputy commissioner of the State Department of Health, as one of its members, this committee specifically considered the roles in tuberculosis control played respectively by the City Health Department, the Boston Sanatorium and the Boston Tuberculosis Association.

A shortage of at least 20 nurses in the City Health Department was demonstrated, — a situation that called for rectification in the interests of adequate home supervision of cases. It was recommended that a well qualified and experienced public-health nurse assume the position of special (nurse) consultant in tuberculosis and that the position of Medical Social Work Supervisor be established in the Boston Health Department. After review of the facts the committee found that the present case-study program was adequate, to the extent that an actual shortage of beds for patients with tuberculosis had become evident.

In regard to the Boston Sanatorium the Committee approved the recommendations of Dr. Teague that a full-time medical director be appointed; that the salary of resident physicians be raised from $3800 to $6000 per year, with new housing on the grounds for an adequate medical staff; that the full bed space be utilized; and that a rehabilitation program be instituted at the Sanatorium.

Concerning the role of the Boston Tuberculosis Association, the committee neither supported nor took issue with Dr. Teague's recommendation that the Prendergast Preventorium be closed — on the ground that it serves a function that should be carried out by the social agencies when parents of children are taken away from the home because of tuberculosis. The committee did, however, go on record as disapproving the support of the Prendergast Preventorium with tuberculosis-seal and other money because "the returns in tuberculosis control are very small in proportion to the money spent." At present the X-ray Unit of the Boston Tuberculosis Association is believed to fulfill a need, although the time was envisaged when this function could be assumed by the City Health Department. If the Boston Tuberculosis Association as a private philanthropic institution were to continue to justify its existence in the future, as it has amply done in the past, it would probably be in the area of rehabilitation, "one of the most important and perhaps one of the most neglected fields of work," and possibly in health education, although it is difficult to define the area of activity in this respect. Dr. Teague

had advocated "a well trained health educator at a salary not less than $5000 a year," whereas the Committee went so far as to recommend support by the Boston Tuberculosis Association of the teaching of tuberculosis and pulmonary disease in medical schools.

FRANKLIN DISTRICT MEDICAL SOCIETY

Among the district-society centennial observances that have so frequently punctuated the record of Massachusetts medicine in recent years, none have been better planned or more enthusiastically executed than that of Franklin. Franklin County, which it was once deemed necessary to protect by a string of thirteen forts from the hostile French and Indians who periodically poured south from the citadel of Montreal, is well known to be one of the state's more geographically extensive and least thickly populated areas.

Such a rural atmosphere and the fact that it is Massachusetts's smallest district society in point of numbers, however, has served only to make the fifty-five physicians who comprise the membership of the society more conscious of their responsibilities, more reliant on their own resources and more conspicuously successful in their solidarity.

The hundredth anniversary of the emergence of the Franklin District as a component part of the Massachusetts Medical Society — splitting off from the still older independent Franklin Medical Association — was celebrated last May at Greenfield.

During the day of May 24 a pageant consisting of twenty exhibits depicting a century of progress in the art of healing was open to the public in the Greenfield Armory; in the evening of May 27 a dinner was held at which Dr. Elmer L. Sevringhaus, clinical professor of medicine at New York Medical College, spoke on "Diagnostic and Therapeutic Aspects of Clinical Nutrition."

On this occasion also, Dr. Lawrence R. Dame, former president of the society, presented a historical sketch of the organization and of many of the physicians who had helped to make medical practice in Franklin County an almost unique institution since 1663, when the county was authorized by the General Court of Massachusetts as the Dedham Grant.

Many of these pioneer physicians had varied interests and were engaged in multiple spheres of usefulness in addition to the practice of medicine. Thus Thomas, the founding father of the famous Williams family, having gone to the French and Indian wars, after his return became justice of the peace and judge of the Court of Common Pleas and of the Court of Probate, as well as town clerk, and father of another physician who became also a military surgeon, secretary and treasurer of the trustees of Deerfield Academy, a justice of the peace and town clerk. And many others of the 523 physicians who have been identified with Franklin County have had similar careers of service to their communities.

Dr. Dame in these annals has drawn the picture of a robust stock that has brought a great nation into the world. The survival of that nation will depend on the survival of the same stock, from whatever rock it may have been originally hewn.

It is getting to be quite common for newspapers to have the first, and sometimes the only, reports of remarkable surgical operations. It is all right enough for the papers to publish medical intelligence; but it would be more consonant with our feelings, and more in accordance with professional etiquette, if medical men would first send the results of their cases to a Medical *Journal.*

Boston M. & S. J., *July 2, 1851*

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

Curtin — J. Frank Curtin, M.D., of North Abington, died on June 4.

Dr. Curtin received his degree from Baltimore Medical College in 1906. He retired in 1949.

Two daughters survive.

Mahoney — Charles F. Mahoney, M.D., of Winthrop, died on June 10. He was in his sixty-ninth year.

Dr. Mahoney received his degree from Tufts College Medical School in 1906. He had been Winthrop school physician for ten years.

His widow, three daughters and a son survive.

OBITUARY

FRANKLIN W. WHITE

Franklin Warren White was born in Boston on October 23, 1869, — the only child of Dr. Elisha Mann White and Amelia Hopkins White. For most of his boyhood he lived in Roxbury. He attended Roxbury Grammar School and Roxbury Latin School, from which he graduated at the age of sixteen. He entered the Massachusetts Institute of Technology as the youngest in his class. As a youth he had many interests. He enjoyed gardening, played the violin, sang solos in church, acted in Shakespearean productions, climbed mountains and sailed. While at M. I. T. he was bacteriologist for the Massachusetts State Board of Health and was sent abroad to investigate water systems. He helped in the establishment of the reservoirs at Framingham.

After his graduation from M. I. T. in 1890, and because of his increasing interest in public health and medicine, he followed the example of his two cousins, Herbert Warren White of Roxbury and Charles Warren White of Fairhaven, and entered Harvard Medical School, from which he graduated in 1895. While at medical school he taught physiology at M. I. T., later becoming the Institute's medical adviser. Then followed appointments as instructor of medicine at Harvard, professor of clinical medicine at Dartmouth, visiting physician at the Infants Hospital in Boston and clinical researcher at the Massachusetts General Hospital. He became a member of the medical staff of the Boston City Hospital and was active there in visiting and consultation work from 1905 to 1950. He was a familiar figure in the wards of the hospital and was always a helpful adviser to house staff, visiting colleagues and students.

Dr. White was a former president of the American Gastroenterological Association and had served as chairman of the Section on Gastroenterology of the American Medical Association and Regent of the American College of Physicians. He was also a member of the Association of American Physicians.

In the American Gastroenterological Association he was not only honored as a former president and as the recipient of the Friedenwald Medal in 1948 but was regarded as one of the elder advisers, whose experience was always blended with a lively interest in the newer projects of gastroenterology. He was a faithful and warmly welcomed attendant at the association's annual meetings.

In his practice as well as in his teaching and clinical studies, in his hours of rest and recreation as well as in his hours of work, and in every aspect of his life Dr. White was the beloved physician who set an unpretentious example to a host of students, colleagues and other acquaintances.

P. D. W.
S. J.

BOSTON MEDICAL LIBRARY

REPORT OF THE PRESIDENT

To the Trustees and Fellows of the Boston Medical Library: I have the honor to present my fifth annual report as President.

The library continues to grow both in number of volumes and in circulation. Since Dr. Viets' message will tell you something about our acquisitions during the year, I want particularly to call your attention to our growth in circulation. Circulation of books is a direct measure of the usefulness of the library. Our growth in this respect during the past five years has been quite remarkable. In 1946 38,226 volumes were taken from the shelves, whereas in 1950 64,256 volumes circulated, an increase of 26,000 volumes, or more than two thirds. This is certainly a clear indication of the need for this great reference library in Massachusetts.

The increase in actual attendance has not been so dramatic; about 3500 more members and nonmembers entered the library in 1950 than in 1946. This simply means that we are sending out more books to physicians' offices, hospitals and libraries than we formerly did. Our interlibrary loans to nonmembers have likewise increased by about 1000 in the five years.

During the year the Massachusetts Medical Society has taken over the building next door and after extensive repairs has now taken occupancy. The trustees voted to allow a doorway to be cut through on the first floor, so that there might be a suitable physical connection between the two buildings. We have executed an agreement, under legal advice, that we believe adequately safeguards the interest of the library. Some rearrangement of space has now become necessary. The *Journal* has taken over the offices formerly occupied by the Treasurer and Dr. Conlin, so that they now use the whole lower floor of the stack building. The *Journal of Bone and Joint Surgery* has taken the offices formerly occupied by the President and Secretary of the Massachusetts Medical Society. Dr. Thorndike's Selective Service committee has taken the rooms formerly occupied by the clerical force and Mr. Boyd. The Massachusetts Medical Society will continue to use John Ware Hall for two Council meetings a year and for the Postgraduate Assembly. I am glad to tell you that the compensation we will now receive from these various tenants will just about equal what we received before.

We rejoice that the three organizations are to continue to live as friendly neighbors and cooperating friends.

Our financial condition is not much changed. We are still slipping along on pretty thin ice. However, there is one cheerful thought. We have reduced our indebtedness to the special funds to a reasonably nominal figure. Another year ought to clear up this troublesome matter. Without the income from the Massachusetts Medical Society members of the library could not carry on. It would have to liquidate its assets or materially change its policy. With our income from restricted funds we might be able to handle our rare-book collection, but to maintain an up-to-date reference library would be out of the question. Our costs continue to rise in spite of the utmost care. We must follow business and industry in wage increases. We have a very loyal staff, but they are human, and their living costs have gone up like those of every other employee, and in all fairness we must meet them. This has put an extra load on our already heavily laden financial structure.

Our income is still further reduced by the resignation of a considerable number of fellows. Their reasons for resigning are many — some move out of the State, others feel the financial pinch as they retire from practice — but a fair number feel that the fellowship is not worth the extra $15 over and above the $5 they pay through the Massachusetts Medical Society.

From a strictly practical point of view we must be fair and say that the fellowship does not bring fifteen dollars' worth of extra service. We wish that some way might be found for library fellowship to carry special privileges. Many schemes have been suggested, such as a sort of literary club with special rooms set apart — an Academy of Medicine and so forth—but none of them have materialized.

Let's look at it another way. Here we have one of the finest and most valuable medical libraries in the world. Thanks to our many benefactors, we have a remarkable collection of clinical medical literature and rare books. Our collection of over 700 incunabula is the largest in any medical library in this country, and our 60 medieval and Renaissance manuscripts, written largely on vellum, are certainly representative in their field. There is also a splendid collection of Hebraica, and the Storer collection of medical medals and coins is unexcelled. This is an addition to our complete collection of periodicals. We fret a little, sometimes, that so much of our income from invested funds (two thirds, to be exact) must be expended for rare items, but without them we could not have a well balanced collection for both clinical and historical research that is well-nigh unexcelled anywhere.

Is it not reasonable to suppose that there are 1000 among the 7000 physicians in Massachusetts who are able and willing to give $15 a year to support this extraordinary institution? Remember that the fellows constitute the corporate body of the library. There must always be a group of fellows to hold and administer the trust funds. The fellows own the library — and a very valuable capital investment it is — of over a million dollars' worth of assets. If the library should be compelled to liquidate, only the fellows would receive the proceeds. One thousand fellows should be our goal — let us all try to make it.

We cannot accomplish this unless we ourselves have faith in the library and are willing to do a little missionary work. Let us take time now and again to explain the library to our fellow members, that they may better appreciate what this great institution means to the Massachusetts Medical Society.

The library celebrated the 75th anniversary of its founding on October 16, 1950, by holding open house during the day and a dinner at the Hotel Kenmore in the evening. Distinguished guests were present from nearly all the leading medical libraries of the country. Dr. Viets acted as toastmaster at the dinner and reminisced pleasantly about the past history of the library. The principal address was given by Dr. Chauncey D. Leake, Ph.D., executive vice-president and dean in charge of the Medical Program at the University of Texas.

Again we owe a debt of gratitude to our librarian, Dr. Viets, our director, Mr. Ballard, and our loyal and hard-working staff for their untiring efforts to give efficient service in the face of considerable odds. We hope that some day the completion of our physical plant will make things easier for them. Again, let me beseech your faith and your loyalty to the Boston Medical Library.

WALTER G. PHIPPEN

CORRESPONDENCE

SURRENDER OF REGISTRATION

To the Editor: At the meeting of the Board of Registration in Medicine held May 18, it was voted to accept the voluntary surrender of registration to practice medicine in this Commonwealth of Dr. Edwin C. Shattuck, 314 County Street, New Bedford, as of April 15, 1951.

ROBERT C. COCHRANE, M.D., *Secretary*

State House
Boston

RESTORATION OF LICENSE

To the Editor: At the meeting of the Board of Registration in Medicine held June 6, it was voted to restore the registration to practice medicine in this Commonwealth to Dr. R. Reyes-Garcia, East Longmeadow and Springfield, Massachusetts, with the provision that he be placed on probation for five (5) years and that he be required to report to the Board annually.

ROBERT C. COCHRANE, M.D., *Secretary*

State House
Boston

BOOK REVIEW

History, University of Vermont College of Medicine. Editor, William A. R. Chapin, M.D., Springfield, Massachusetts. Associate editor, Lyman Allen, M.D., Burlington, Vermont. 8°, cloth, 162 pp., with frontispiece and illustrations. Hanover, New Hampshire: Dartmouth Printing Company, 1951. $5.00.

This book gives a good picture of the University of Vermont College of Medicine.

There is a description of the events — and difficulties — leading to the original formation of the school in 1804. There are photographs and personal sketches of various worthies who played a part in molding its personality after its more formal reopening forty-nine years later. Most of them are depicted as wearing beards and all have strong, rugged faces that suggest that a New England conscience, made all the more stubborn by life in the Green Mountains, must have become an inherited tradition.

There are stories of the early days, of how medicine was taught and practiced in what was a New England frontier, and stories, too, of the pranks and the kind of student mischief that was prevalent when the school was establishing its footing.

There is a war record that proves that graduates of the University of Vermont School of Medicine have always been ready to serve the country in times of need. There is an account of how the school became coeducational. There is a description of what the school is today, showing how eagerly it continues to strive to educate good physicians who will practice good medicine wherever they decide to live.

Anyone who is interested in the history of one of the enduring New England medical schools will enjoy this book. It will appeal particularly to the reader who knows the countryside around Burlington and Lake Champlain and the charm of the university, with its campus, its old buildings and the air it now has of being as much an integral part of Vermont as are the mountains themselves.

R. Fitz, M.D.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Facts about the Menopause. By Maxine Davis. 8°, cloth, 172 pp. New York, New York: McGraw-Hill Book Company, Inc., 1951. $2.50.

This is a popular book on a subject of vital interest to all women. The author has prepared her text with the assistance of a number of physicians. There is a good index, and the publishing is well done.

Surgical Nursing. By Eldridge L. Eliason, M.D., Sc.D., consulting surgeon, Hospital of the University of Pennsylvania and Presbyterian and Philadelphia General hospitals; L. Kraeer Ferguson, M.D., professor of surgery, University of Pennsylvania and Woman's Medical College of Pennsylvania, surgeon, Graduate Hospital of the University of Pennsylvania, Hospital of the Woman's Medical College of Pennsylvania, Philadelphia General Hospital and Doctors Hospital, and consulting surgeon, Frankford Hospital and United States Naval Hospital, Philadelphia; and Lillian A. Sholtis, R. N., M. S., assistant professor of surgical nursing, Yale University School of Nursing. Ninth edition. 8°, cloth, 728 pp., with 336 illustrations. Philadelphia: J. B. Lippincott Company, 1950. $4.00.

In this new edition a standard textbook has been almost entirely rewritten and brought up to date since the publication of the previous edition in 1947. The material is well arranged and well written. The first part is devoted to surgical nursing in general. The following parts are devoted to special systems of the body. The concluding part discusses operative aseptic technic. There is a comprehensive index and the book is well published. It is unfortunate that important material is printed on the front and back covers of the binding, since the first and last parts of any volume receive the hardest usage.

The National Formulary: National Formulary IX: N.F.IX: Prepared by the Committee on National Formulary under the supervision of the Council, by authority of the American Pharmaceutical Association. Official from November 1, 1950. 8°, cloth, 877 pp. Washington, D.C.: American Pharmaceutical Association, 1950. $8.00.

This new edition of a standard authoritative reference work has been thoroughly revised and brought up to date. It represents the work of four years of the special committee of the American Pharmaceutical Association and hundreds of collaborators. It is an essential reference work for all medical libraries and druggists.

The Urinary Function of the Kidney. By A. V. Wolf, Ph.D., associate professor of physiology, Albany Medical College, Union University. 8°, cloth, 363 pp. New York: Grune and Stratton, 1950. $7.50.

This comprehensive monograph discusses all aspects of the urinary function of the kidney. There are special chapters on diuresis and diuretics and antidiuresis and antidiuretics and on the endocrines in urinary function. The literature on the subject is discussed throughout the text. A bibliography of 1189 references concludes the text. There is a good index, and the publishing is excellent. The monograph should be in all medical libraries and in all collections on physiology and renal diseases.

Über Fortschritt und Grenzen ärztlicher Wissenschaft und Praxis. By Simon Bollag. 8°, paper, 27 pp. Basel: Benno Schwabe and Company, 1950. Broschiert Fr. 3. (Distributed by Grune and Stratton, New York.)

This short philosophic essay discusses the status of internal therapy of the present time, the origin and ways of scientific research in medicine and the conception of disease in the first half of the twentieth century.

The Cytology and Life-History of Bacteria. By K. A. Bisset, Ph.D., lecturer in bacteriology, University of Birmingham. 8°, cloth, 136 pp., with 43 illustrations. Baltimore: Williams and Wilkins Company, 1950. $3.50.

The author in this monograph attempts to present a reasoned case for regarding bacteria as living cells with the same structure and other functions as other living cells. No attempt has been made to review the literature on bacterial cytology. The bibliographies appended to the various chapters are confined to the recent literature. There is a good index, and the book is well published. It should be in all collections on bacteriology.

Steroid Hormones and Tumors: Tumorigenic and antitumorigenic actions of steroid hormones and the steroid homeostasis: Experimental aspects. By Alexander Lipschutz, M.D., director, Department of Experimental Medicine, National Health Service of Chile. 8°, cloth, 309 pp., with 111 illustrations. Baltimore: Williams and Wilkins Company, 1950. $6.00.

Since 1936 the author and his associates have been concerned with the problem of the production and inhibition of tumoral growth by steroids. A series of papers have been published, but many of the findings have been described only in a thesis of the University of Chile or not at all. This monograph brings together in a condensed form all the work accomplished during the last fifteen years. Included are comparative summaries of the work on estrogen-induced tumors done since 1932. The text is divided into three main parts: the tumorigenic action of steroids and its implication for the problem of cancer; the antitumorigenic action of steroids; and the steroid balance, or steroid homeostasis, and the antitumoral autodefense. A comprehensive survey of the pertinent literature has been made, and a bibliography of forty pages is appended to the text. There are indexes of authors and subjects, and the monograph is well published. It should be in all collections on tumors and hormones.

Medizinische Psychologie. By Ernst Kretschmer, Dr. Med., Dr. Phil. h.c.,o., professor of psychiatry aud neurology, Tübingen. Tenth edition. 8°, cloth, 304 pp., with 26 illustrations. Stuttgart: Georg Thieme, 1950. Ganzleinen DM 24.

This standard textbook on medical psychology has been revised and brought up to date. The text is divided into five parts: the function of the mind, the apparatus of the mind, impulse and temperament, personality and reactive types, and psychotherapy. There is a good index; the book is well published. It should be in all collections on the subject.

Studies in Lobotomy. Milton Greenblatt, M.D., Robert Arnot, M.D., and Harry C. Solomon, M.D., editors. 8°, cloth, 495 pp. New York: Grune and Stratton, 1950. $10.00.

Twenty-seven physicians have contributed to this volume based on the experience gained at the Boston Psychopathic Hospital, where the operation of lobotomy was begun in November, 1943. The text is divided into two main parts: clinical considerations and special studies. Dr. Greenblatt gives a review of the recent literature on psychosurgery and in co-operation with Drs. Talbot and Arnot presents a follow-up study of one to four years in 205 cases of bilateral prefrontal lobotomy. Short lists of selected references are appended to the various chapters, and there is a good subject index. The book is well published and should be in all collections on psychiatry and brain surgery.

Orthopaedic Surgery. By Walter Mercer, M.B., Ch.B., F.R.C.S. (Edin.), F.R.S. (Edin.), professor of orthopedic surgery, University of Edinburgh, and director of orthopedic services to the South-Eastern Regional Hospital Board, Scotland. With a foreword by Sir John Fraser, Bart., K.C.V.O., M.C., F.R.S. Ed., F.R.C.S. Ed., M.D., Ch.M., F.R.A.C.S., Regius Professor of Clinical Surgery, University of Edinburgh. Fourth edition. 8°, cloth, 1016 pp., with 427 illustrations. Baltimore: Williams and Wilkins Company, 1950. $10.00.

Dr. Mercer has revised this new edition to bring the material up to date. The chapters on general affections of the skeleton, venereal disease, arthritis, affections of the spine and complications of trauma have been rewritten. A bibliography arranged by subjects concludes the text, and there is a good index. The printing was done in Great Britain, and the publishing is excellent. The book is recommended for all orthopedic collections.

A Text-Book of X-Ray Diagnosis: By British authors. In four volumes. Second edition. Edited by S. Cochrane Shanks, M.D., F.R.C.P., F.F.R., director, X-ray Diagnostic Department, University College Hospital, London; and Peter Kerley, M.D., F.R.C.P., F.F.R., D.M.R.E., director, X-ray Department, Westminster Hospital, and radiologist, Royal Chest Hospital, London. Volume III. 8°, cloth, 830 pp., with 694 illustrations. Philadelphia: W. B. Saunders Company, 1950. $18.00.

The third volume of this comprehensive treatise is devoted to the alimentary tract, billary tract, abdomen, radiology in obstetrics and gynecology and urinary tract. Seventeen specialists contributed to the volume. The text is well documented with references to the pertinent literature. There is a good index, and the publishing is excellent. The treatise when finished will furnish in four volumes a view of the current status of the subject in Great Britain. The set of four volumes should be in all collections in radiology.

Pediatric X-Ray Diagnosis: A textbook for students and practitioners of pediatrics, surgery and radiology. By John Caffey, M.D., professor of clinical pediatrics, Columbia University, College of Physicians and Surgeons, attending pediatrician and roentgenologist, Babies Hospital and Vanderbilt Clinic, New York City, consulting pediatrician, Grasslands Hospital, Westchester County, New York, and New Rochelle Hospital, New Rochelle, New York, consulting roentgenologist, Orange Memorial Hospital, Orange, New Jersey, and consultant in pediatric roentgenology, New York Hospital, New York City. Second edition. 4°, cloth, 862 pp., with 1039 illustrations. Chicago: Year Book Publishers, Incorporated, 1950. $22.50.

This comprehensive treatise, first published in 1945, has been thoroughly revised and brought up to date. Many subjects have been added, and several sections have been rewritten and many others expanded. A large number of references have been added to the lists appended to the various subjects. There is a good index, and the publishing is excellent. The book should be in all collections on pediatrics and radiology.

Textbook of Abnormal Psychology. By Roy M. Dorcus, professor of psychology and division dean of life sciences, University of California, and professor of psychology, University of California School of Medicine, Los Angeles, California; and G. Wilson Shaffer, dean of the University, professor of psychology, director of the Psychological Clinic, Johns Hopkins University, and chief psychologist, Sheppard-Enoch Pratt Hospital, Towson, Maryland. Fourth edition. 8°, cloth, 717 pp., with 38 illustrations. Baltimore: Williams and Wilkins Company, 1950. $5.00.

This textbook has enjoyed an enviable publication record. First printed in 1934, it has now gone through four editions, with fifteen printings. Three chapters have been added: brain damage disorders; psychosomatic disorders; and the history of mental disease. The section on psychotherapy has been practically rewritten. The results of recent research have been incorporated throughout the text. The book constitutes a survey based on a bibliography of 1200 references appended to the text. There are indexes of authors and subjects, and the book is well published. It should be in all medical libraries and in all collections on the subject.

McClung's Handbook of Microscopical Technique for Workers in Animal and Plant Tissues. By thirty-five authors. Edited by Ruth McC. Jones, professor of biology, Winthrop College, South Carolina. Third edition, revised and enlarged. 8°, cloth, 790 pp., with 157 illustrations. New York: Paul B. Hoeber, Incorporated, 1950. $12.00.

This standard reference book is the joint work of a large number of specialists in their particular fields. The new edition has been revised by the addition of descriptions of many new methods. New material includes a discussion of the phase microscope and its application to biologic materials; the preparation of materials for electron microscopy; the radioautographic method; and polarization microscopy. Material on embedding has been added, and the text in general has been extensively revised.

References to the pertinent literature are carried as footnotes on the appropriate pages. There is an extensive index, and the book is well published. It should be in the reference sections of all medical libraries and in special collections on microscopy.

NOTICES

ANNOUNCEMENT

Dr. Lester H. Tobin announces the opening of his office for the practice of internal medicine and hematology at 29 Broad Street, Lynn.

INTERNATIONAL CONGRESS OF PHYSICAL MEDICINE

The International Congress of Physical Medicine will be held in London July 14 to 19, 1952. The meetings of the Congress will feature discussions of the clinical, remedial, prophylactic and educational aspects of physical medicine and the diagnostic and therapeutic methods employed in physical medicine and rehabilitation. Technical, scientific and historical exhibitions also will be arranged. In addition to the scientific program, a full program of social events and entertainment is being planned for the members and associate members. Arrangements for visits of scientific and historical interest to London and the provinces are also being made for the Congress week and the following week.

Full details concerning the meetings will be published later. Applications for the provisional program should be addressed to the Honorary Secretary, International Congress of Physical Medicine (1952), 45, Lincoln's Inn Fields, London, W.C.2.

(Notices concluded on page xv)